```
=> fil reg
FILE 'REGISTRY' ENTERED AT 09:04:35 ON 29 JAN 2002
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STRUCTURE FILE UPDATES:   28 JAN 2002  HIGHEST RN 387816-30-0
DICTIONARY FILE UPDATES:  28 JAN 2002  HIGHEST RN 387816-30-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02.  Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved.  Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies.  Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

=> d ide can tot

L66  ANSWER 1 OF 10  REGISTRY  COPYRIGHT 2002 ACS
RN   329967-85-3  REGISTRY
CN   Synthetase, prostaglandin endoperoxide, 1 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Arachidonate cyclooxygenase 1
CN   COX-1
CN   Cyclooxygenase 1
CN   Prostaglandin endoperoxide synthetase 1
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             208 REFERENCES IN FILE CA (1967 TO DATE)
             211 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:68442

REFERENCE   2:  136:65550

REFERENCE   3:  136:64576

REFERENCE   4:  136:63779

REFERENCE   5:  136:63770

REFERENCE   6:  136:49587
```

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

REFERENCE 7: 136:49576

REFERENCE 8: 136:48407

REFERENCE 9: 136:48271

REFERENCE 10: 136:48168

L66 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN 329900-75-6 REGISTRY
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Arachidonate cyclooxygenase 2
CN COX 2
CN **Cyclooxygenase 2**
CN Prostaglandin endoperoxide synthase-2
CN Prostaglandin endoperoxide synthetase 2
CN Prostaglandin G/H synthase-2
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
714 REFERENCES IN FILE CA (1967 TO DATE)
733 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:69808

REFERENCE 2: 136:69730

REFERENCE 3: 136:68721

REFERENCE 4: 136:68645

REFERENCE 5: 136:68589

REFERENCE 6: 136:68442

REFERENCE 7: 136:68142

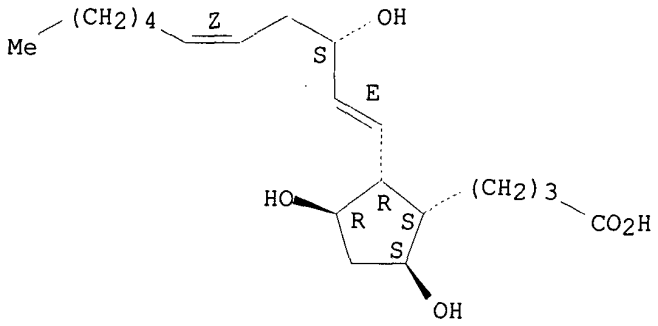
REFERENCE 8: 136:67990

REFERENCE 9: 136:67775

REFERENCE 10: 136:67614

L66 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN 219566-52-6 REGISTRY
CN Cyclopentanebutanoic acid, 3,5-dihydroxy-2-[(1E,3S,5Z)-3-hydroxy-1,5-undecadienyl]-, (1S,2R,3R,5S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **IPF2.alpha.-V**
CN **Isoprostane IPF2.alpha.-V**
FS STEREOSEARCH
MF C20 H34 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

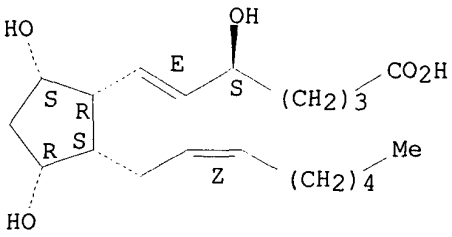
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:322440

REFERENCE 2: 130:95398

L66 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN **214894-56-1** REGISTRY
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-,
(5S,6E,9.alpha.,11.alpha.,12.alpha.,14Z)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H34 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:178987

REFERENCE 2: 135:3903

REFERENCE 3: 134:278955

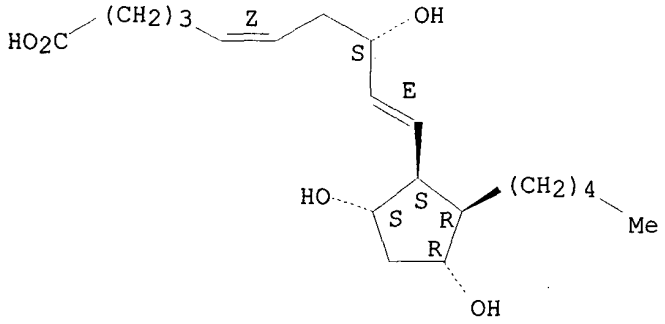
REFERENCE 4: 134:278954

REFERENCE 5: 130:61215

REFERENCE 6: 129:316057

L66 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN **190664-75-6** REGISTRY
CN 5,9-Decadienoic acid, 10-[(1S,2R,3R,5S)-3,5-dihydroxy-2-pentylcyclopentyl]-8-hydroxy-, (5Z,8S,9E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,9-Decadienoic acid, 10-(3,5-dihydroxy-2-pentylcyclopentyl)-8-hydroxy-, [1S-[1.alpha.(5Z,8R*,9E),2.alpha.,3.beta.,5.beta.]]-
OTHER NAMES:
CN 8-F2t-Isoprostane
CN **IPF2.alpha.-III**
CN **Isoprostane IPF2.alpha.-III**
FS STEREOSEARCH
MF C20 H34 O5
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:255598

REFERENCE 2: 135:57207

REFERENCE 3: 134:310229

REFERENCE 4: 134:266111

REFERENCE 5: 132:217250

REFERENCE 6: 131:281919

REFERENCE 7: 131:227155

REFERENCE 8: 130:262541

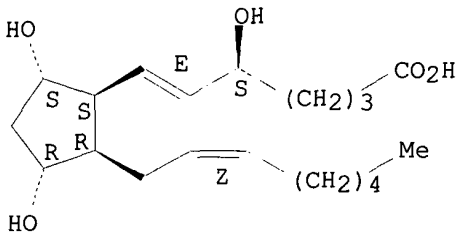
REFERENCE 9: 130:250679

REFERENCE 10: 127:17515

L66 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN **180469-63-0** REGISTRY
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **IPF2.alpha.-I**
CN **Isoprostane IPF2.alpha.-I**

FS STEREOSEARCH
MF C20 H34 O5
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, TOXCENTER, TOXLIT

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1967 TO DATE)
11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:57207

REFERENCE 2: 134:310229

REFERENCE 3: 131:336832

REFERENCE 4: 131:227155

REFERENCE 5: 130:250679

REFERENCE 6: 130:166709

REFERENCE 7: 130:61215

REFERENCE 8: 129:310983

REFERENCE 9: 129:662

REFERENCE 10: 127:344749

L66 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN **39391-18-9** REGISTRY
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Arachidonate cyclooxygenase
CN Arachidonic acid cyclooxygenase
CN Arachidonic cyclooxygenase
CN **Cyclooxygenase**
CN E.C. 1.14.99.1
CN Fatty acid cyclooxygenase
CN Gene TIS10 proteins
CN Peroxidase, prostaglandin hydroperoxide
CN PG synthetase
CN PGG/H synthase
CN PGG2 peroxidase
CN PGH synthase
CN PGH2 synthase
CN PGH2 synthetase
CN PGI2 cyclooxygenase
CN Prostaglandin cyclooxygenase
CN Prostaglandin endoperoxide G/H synthase

CN Prostaglandin endoperoxide H synthase
CN Prostaglandin endoperoxide synthase
CN Prostaglandin endoperoxide synthetase
CN Prostaglandin G/H synthase
CN Prostaglandin G2 peroxidase
CN Prostaglandin G2/H2 synthase
CN Prostaglandin H synthase
CN Prostaglandin H synthetase
CN Prostaglandin H2 synthase
CN Prostaglandin H2 synthetase
CN Prostaglandin hydroperoxidase
CN Prostaglandin hydroperoxide peroxidase
CN Prostaglandin peroxidase
CN Proteins, specific or class, gene TIS10
CN TXA2 cyclooxygenase
DR 59763-19-8, 64427-82-3, 69913-02-6
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, EMBASE, NIOSHTIC, PROMT, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7172 REFERENCES IN FILE CA (1967 TO DATE)
73 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7158 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:67410

REFERENCE 2: 136:67126

REFERENCE 3: 136:66317

REFERENCE 4: 136:65408

REFERENCE 5: 136:64557

REFERENCE 6: 136:63427

REFERENCE 7: 136:58848

REFERENCE 8: 136:52191

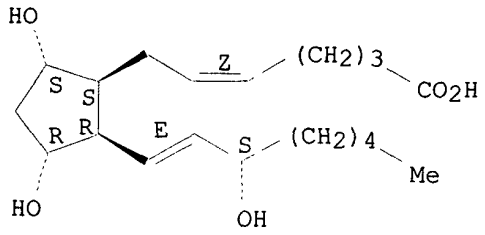
REFERENCE 9: 136:48206

REFERENCE 10: 136:47985

L66 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN **27415-26-5** REGISTRY
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]- (8CI)
OTHER NAMES:
CN 15-F2t-Isoprostane
CN 8-epi-PGF2.alpha.
CN 8-epi-Prostaglandin F2.alpha.
CN 8-Iso-PGF2.alpha.
CN 8-iso-Prostaglandin F2.alpha.
CN 8-Isoprostaglandin F2.alpha.
CN **Isoprostaglandin F2.alpha. type-III**
FS STEREOSEARCH
MF C20 H34 O5
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, MEDLINE,

TOXCENTER, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

301 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
301 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:68019

REFERENCE 2: 136:52094

REFERENCE 3: 136:48283

REFERENCE 4: 136:35820

REFERENCE 5: 136:32971

REFERENCE 6: 136:32053

REFERENCE 7: 136:16442

REFERENCE 8: 136:4645

REFERENCE 9: 136:3973

REFERENCE 10: 135:370126

L66 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN **7782-44-7** REGISTRY
CN Oxygen (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Dioxygen
CN Molecular oxygen
CN Oxygen molecule
FS 3D CONCORD
DR 1338-93-8, 14797-70-7, 80217-98-7, 80937-33-3
MF O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, TRCTHERMO*, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

O=O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

262107 REFERENCES IN FILE CA (1967 TO DATE)
20212 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
262385 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:79007

REFERENCE 2: 136:79002

REFERENCE 3: 136:78942

REFERENCE 4: 136:78935

REFERENCE 5: 136:78730

REFERENCE 6: 136:78483

REFERENCE 7: 136:78463

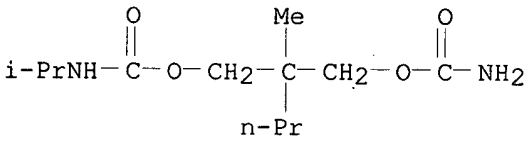
REFERENCE 8: 136:78456

REFERENCE 9: 136:78448

REFERENCE 10: 136:78433

L66 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2002 ACS
RN **78-44-4** REGISTRY
CN Carbamic acid, (1-methylethyl)-, 2-[[(aminocarbonyl)oxy]methyl]-2-methylpentyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Carbamic acid, isopropyl-, 2-(hydroxymethyl)-2-methylpentyl ester, carbamate (6CI)
CN Carbamic acid, isopropyl-, 2-(hydroxymethyl)-2-methylpentyl ester carbamate (ester) (8CI)
OTHER NAMES:
CN 2-Methyl-2-propyl-1,3-propanediol carbamate isopropylcarbamate
CN Apesan
CN Atonalyt
CN Calenfa
CN Caprodat
CN Carisol
CN Carisoma
CN Carisoprodate
CN Carisoprodatum
CN Carisoprodol
CN Domarax
CN Flexal
CN Flexartal
CN Isobamate
CN Isomeprobamate
CN Isopropyl meprobamate
CN Isoprotan
CN Isoprotane
CN Isoprothane
CN Izoprotan
CN Miolisodal
CN Mioril
CN N-Isopropyl-2-methyl-2-propyl-1,3-propanediol dicarbamate

CN Rela
CN Relasom
CN Sanoma
CN Skutamil
CN Soma
CN Somadril
CN Somalgit
CN Stialgin
FS 3D CONCORD
DR 8053-63-2
MF C12 H24 N2 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

162 REFERENCES IN FILE CA (1967 TO DATE)
162 REFERENCES IN FILE CAPLUS (1967 TO DATE)
21 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:322726

REFERENCE 2: 135:231801

REFERENCE 3: 135:210730

REFERENCE 4: 134:362292

REFERENCE 5: 134:349093

REFERENCE 6: 134:290275

REFERENCE 7: 134:127102

REFERENCE 8: 134:26229

REFERENCE 9: 133:292058

REFERENCE 10: 133:3389

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:04:46 ON 29 JAN 2002
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FILE COVERS 1907 - 29 Jan 2002 VOL 136 ISS 5
FILE LAST UPDATED: 28 Jan 2002 (20020128/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGlstRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1907 to the present. Bibliographic information and abstracts were added in 2001 for over 3.8 million records from 1907-1966.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

=> d all hitstr tot 164

L64 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:384464 HCAPLUS
DN 133:3389
TI **Methods** and compositions for **determining** lipid peroxidation levels in oxidant stress syndromes and diseases
IN **Fitzgerald, Garret A.; Rokach, Joshua; Pratico, Domenico; Trojanowski, John Q.**
PA The Trustees of the University of Pennsylvania, USA; Florida Institute of Technology
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM C12P031-00
ICS C12Q001-26; G01N033-53
CC 14-10 (Mammalian Pathological Biochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032805	A1	20000608	WO 1999-US28583	19991202 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1135519	A1	20010926	EP 1999-965096	19991202 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1998-110569	P	19981202 <--		
	WO 1999-US28583	W	19991202		

AB The invention includes methods useful for the diagnosis of Alzheimer's disease and the evaluation of enhanced levels of lipid peroxidn. in a mammal. The methods utilize **isoprostanes** as sensitive and stable mol. markers for lipid peroxidn. in a mammal. Methods of identifying compds. useful for the treatment of Alzheimer's disease or for

reducing levels of lipid peroxidn. in a mammal are also included. The invention also includes kits useful for the diagnosis of Alzheimer's disease and for the evaluation of levels of lipid peroxidn. in a mammal.

ST diagnosis Alzheimers disease lipid peroxidn

IT Peroxidation
(lipid; methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

IT Alzheimer's disease
Blood analysis
Body fluid
Cerebrospinal fluid
Diagnosis
Immunoassay
Inflammation
Urine analysis
(methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

IT Antioxidants
(mol. markers; methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

IT **39391-18-9**, Cyclooxygenase
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

IT **78-44-4, Isoprotane**
RL: ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(mol. markers; methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

IT **7782-44-7**, Oxygen, biological studies
RL: ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(reactive; methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Adiyaman; Analytical Biochemistry 1998, V262(1), P45 HCAPLUS
(2) Morrow; US 5891622 A 1999 HCAPLUS
(3) Morrow; Prog Lipid Research 1997, V36(1), P1 HCAPLUS
(4) Practico; FASEB Journal 1998, V12(15), P1777
(5) Practico; Proc Natl Acad Sci USA 1998, V95(7), P3449
(6) Roberts; US 5858696 A 1999 HCAPLUS
(7) Roberts; US 5945295 A 1999 HCAPLUS

IT **39391-18-9**, Cyclooxygenase
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

RN 39391-18-9 HCAPLUS

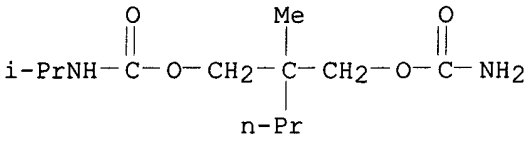
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **78-44-4, Isoprotane**
RL: ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(mol. markers; methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)

RN 78-44-4 HCAPLUS

CN Carbamic acid, (1-methylethyl)-, 2-[[(aminocarbonyl)oxy]methyl]-2-methylpentyl ester (9CI) (CA INDEX NAME)



IT **7782-44-7**, Oxygen, biological studies
RL: ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(reactive; methods and compns. for detg. lipid peroxidn. levels in oxidant stress syndromes and diseases)
RN 7782-44-7 HCAPLUS
CN Oxygen (8CI, 9CI) (CA INDEX NAME)

L64 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:379840 HCAPLUS
DN 131:228560
TI **Isoprostanes**: Chemistry and biological significance
AU **Rokach, Joshua**; Khanapure, Subhash P.; Hwang, Seong-Woo; Adiyaman, Mustafa; Elmir, Zaher; Lawson, John A.; **FitzGerald, Garret A.**
CS Claude Pepper Institute and Department of Chemistry, Florida Institute of Technology, Melbourne, FL, 32901, USA
SO Recent Res. Dev. Org. Chem. (**1998**), 2(Pt. 2), 393-407
CODEN: RDOCFJ
PB Transworld Research Network
DT Journal; General Review
LA English
CC 26-0 (Biomolecules and Their Synthetic Analogs)
AB A review with 53 refs.
ST **review isoprostane** chem biol
IT Prostaglandins
RL: BPR (Biological process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**isoprostanes**; chem. and biol. significance of **isoprostanes**)
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L64 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:36425 HCAPLUS
DN 130:250679
TI Increased formation of distinct F2 **isoprostanes** in hypercholesterolemia
AU Reilly, Muredach P.; **Pratico, Domenico**; Delanty, Norman; DiMinno, Giovanni; Tremoli, Elena; Rader, Daniel; Kapoor, Shiv; **Rokach, Joshua**; Lawson, John; **FitzGerald, Garret A.**
CS Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, USA
SO Circulation (**1998**), 98(25), 2822-2828
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 14-14 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB F2 **isoprostanes** are stable, free radical-catalyzed products of arachidonic acid that reflect lipid peroxidn. in vivo. Specific assays were developed by use of mass spectrometry for the F2 **isoprostanes** **iPF2.alpha.-III** and **iPF2.alpha.-VI** and arachidonic acid (AA). Urinary excretion of the two F2 **isoprostanes** was increased in hypercholesterolemic patients, whereas substrate AA in urine did not differ between the groups. **IPF2.alpha.-III** (pmol/mmol creatinine) was elevated in homozygous familial hypercholesterolemic (HFH) patients (85) compared with age- and sex-matched normocholesterolemic control subjects (58), as were levels of **iPF2.alpha.-VI** (281 vs. 175). Serum cholesterol correlated with urinary **iPF2.**

alpha.-III and **iPF2.alpha.-VI** in HFH patients. Urinary excretion of **iPF2.alpha.-III** (81 vs. 59) and **iPF2.alpha.-VI** (195 vs. 149) was also increased in moderately hypercholesterolemic subjects compared with their controls. Urinary excretion of **iPF2.alpha.-III** and **iPF2.alpha.-VI** was correlated. LDL **iPF2.alpha.-III** levels (ng/mg arachidonate) were elevated in HFH patients compared with controls. The concns. of **iPF2-III** in LDL and urine were significantly correlated in HFH patients. Thus asymptomatic patients with moderate and severe hypercholesterolemia have evidence of oxidant stress in vivo.

ST F2 **isoprostane** blood urine hypercholesterolemia oxidant stress

IT Low-density lipoproteins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**iPF2.alpha.-III**-contg.; increased formation of distinct F2 **isoprostanes** in hypercholesterolemia in humans)

IT Hypercholesterolemia
Lipid peroxidation
Oxidative stress (biological)
Urine
(increased formation of distinct F2 **isoprostanes** in hypercholesterolemia in humans)

IT Blood cholesterol
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(increased formation of distinct F2 **isoprostanes** in hypercholesterolemia in humans)

IT 506-32-1, Arachidonic acid **180469-63-0 190664-75-6, IPF2.alpha.-III**
RL: BOC (Biological occurrence); BIOL (Biological study); **OCCU (Occurrence)**
(increased formation of distinct F2 **isoprostanes** in hypercholesterolemia in humans)

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD

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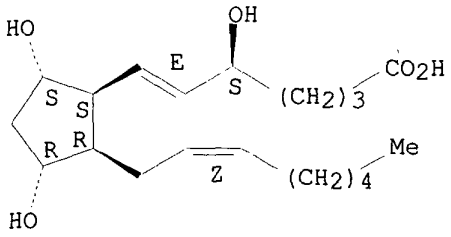
IT **180469-63-0 190664-75-6, IPF2.alpha.-III**
RL: BOC (Biological occurrence); BIOL (Biological study); **OCCU (Occurrence)**
(increased formation of distinct F2 **isoprostanes** in hypercholesterolemia in humans)

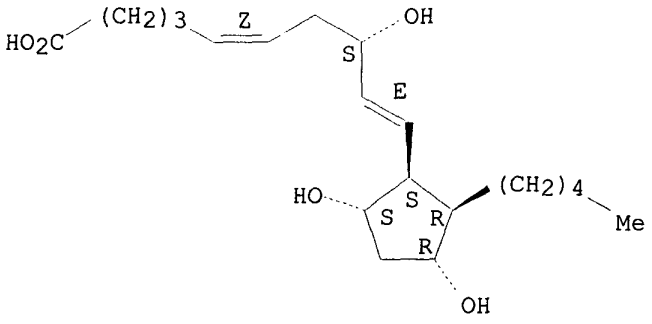
RN 180469-63-0 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 190664-75-6 HCAPLUS
CN 5,9-Decadienoic acid, 10-[(1S,2R,3R,5S)-3,5-dihydroxy-2-pentylcyclopentyl]-8-hydroxy-, (5Z,8S,9E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L64 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:801898 HCAPLUS
DN 130:166709
TI Increased F2-**isoprostanes** in Alzheimer's disease: **evidence** for enhanced lipid peroxidation in vivo
AU **Pratico, Domenico**; Lee, Virginia M.-Y.; **Trojanowski, John Q.**; **Rokach, Joshua**; **Fitzgerald, Garret A.**
CS The Center for Experimental Therapeutics, School of Medicine, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO FASEB J. (**1998**), 12(15), 1777-1783
CODEN: FAJOEC; ISSN: 0892-6638
PB Federation of American Societies for Experimental Biology
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB Alzheimer's disease (AD) includes a group of dementing neurodegenerative disorders that have diverse etiologies but the same hallmark brain lesions. Since oxidative stress may play a role in the pathogenesis of AD and **isoprostanes** are chem. stable peroxidn. products of arachidonic acid, the authors measured both **iPF2.alpha.-III** and **iPF2.alpha.-VI** using gas chromatog.-mass spectrometry in AD and control brains. The levels of both **isoprostanes**, but not of 6-keto PGF1**.alpha.**, an index of prostaglandin prodn., were markedly elevated in both frontal and temporal poles of AD brains compared to the corresponding cerebella. Levels were also elevated compared to corresponding areas of brains from patients who had died with schizophrenia or Parkinson's disease or from nonneuropsychiatric disorders. **IPF2.alpha.**-IV, but not **iPF2.alpha.-III**, levels were higher in ventricular CSF of AD brains relative to the non-AD brains. These data suggest that specific **isoprostane** anal. may reflect increased oxidative stress in AD.
ST **isoprostane** brain Alzheimer disease lipid peroxidn
IT Brain
(areas; increased brain F2-**isoprostanes** in Alzheimer's disease in humans in relation to lipid peroxidn.)
IT Alzheimer's disease
Cerebellum
Frontal cortex
Lipid peroxidation
Oxidative stress (biological)
Parkinson's disease
Schizophrenia
Temporal cortex
(increased brain F2-**isoprostanes** in Alzheimer's disease in humans in relation to lipid peroxidn.)
IT Prostaglandins
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(increased brain F2-**isoprostanes** in Alzheimer's disease in humans in relation to lipid peroxidn.)
IT Cerebrospinal fluid
(ventricular; increased brain F2-**isoprostanes** in Alzheimer's disease in humans in relation to lipid peroxidn.)
IT 506-32-1D, Arachidonic acid, peroxidn. products **27415-26-5**
58962-34-8, 6-Keto PGF1.alpha. **180469-63-0**
RL: BOC (Biological occurrence); BIOL (Biological study); **OCCU (Occurrence)**
(increased brain F2-**isoprostanes** in Alzheimer's disease in humans in relation to lipid peroxidn.)
IT 35121-78-9, PGI2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(increased brain F2-**isoprostanes** in Alzheimer's disease in humans in relation to lipid peroxidn.)
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
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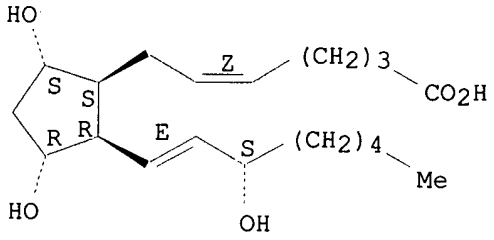
IT **27415-26-5 180469-63-0**
RL: BOC (Biological occurrence); BIOL (Biological study); **OCCU (Occurrence)**
(increased brain F2-**isoprostanes** in Alzheimer's disease in humans in relation to lipid peroxidn.)

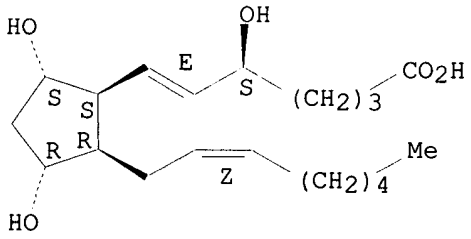
RN 27415-26-5 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 180469-63-0 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L64 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:736922 HCAPLUS
DN 130:61215
TI **Identification** of two major F2 **isoprostanes**, 8,12-iso- and 5-epi-8,12-iso-**isoprostane** F2.alpha.-VI, in human urine
AU Lawson, John A.; Li, Hongwei; **Rokach, Joshua**; Adiyaman, Mustafa; Hwang, Seong-Woo; Khanapure, Subhash P.; **FitzGerald, Garret A.**
CS Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, 19104-6100, USA
SO J. Biol. Chem. (**1998**), 273(45), 29295-29301
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 2-1 (Mammalian Hormones)
AB **Isoprostanes** (iPs) are nonenzymic, free radical-derived compds. isomeric with enzymically formed eicosanoids such as prostaglandins, leukotrienes, and thromboxanes. One group formed by the auto-oxidn. of arachidonic acid, the F2-iPs, consists of four classes of isomers of prostaglandin F2.**alpha**. (PGF2.**alpha**.). They are relatively abundant in human urine. This fact, along with their chem. stability and excellent characteristics for quantitation by gas chromatog./mass spectrometry, has made them attractive indexes of oxidative stress in humans. We developed a specific assay using gas chromatog./mass spectrometry for the first identified F2-iP, **iPF2 .alpha.-III** (previously called 8-iso-PGF2. **alpha**. or 8-epi-PGF2.**alpha**.), which demonstrated the utility of monitoring a specific isomer. Recently, we described an assay for another isomer, **iPF2.alpha.-VI**, which is present in urine in greater concn. than **iPF2.alpha.-III** and which is particularly amenable to quantitation. We now describe the identification in human urine of two more isomers, **8 ,12-iso-iPF2.alpha.-VI** and 5-epi-**8,12-iso-iPF2. alpha.-VI**, using high performance liq. chromatog./tandem

mass spectrometry and gas chromatog./mass spectrometry. These compds. are each present in .apprx.5-fold greater concns. than **iPF2.** **alpha.-VI** (.apprx.20-fold greater than **iPF2.** **alpha.-III**). They share the unique chem. characteristics of class **VI** compds., which make them attractive targets for quantitation by gas chromatog./mass spectrometry and immunoassay development.

ST **isoprostane** F2 detn urine; gas chromatog **isoprostane** F2 urine; mass spectrometry **isoprostane** F2 urine

IT Gas chromatography
Mass spectrometry
Urine
Urine analysis
(8,12-iso- and 5-epi-8,12-iso-**isoprostane** F2.alpha.-VI detection in human urine by gas chromatog./mass spectrometry)

IT Prostanoids
RL: ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(**isoprostanes**; 8,12-iso- and 5-epi-8,12-iso-**isoprostane** F2.alpha.-VI detection in human urine by gas chromatog./mass spectrometry)

IT **27415-26-5**, 8-Iso-PGF2.alpha. **180469-63-0** 197151-20-5 **214894-56-1**
RL: **ANT (Analyte)**; BOC (Biological occurrence); **ANST (Analytical study)**; BIOL (Biological study); **OCCU (Occurrence)**
(8,12-iso- and 5-epi-8,12-iso-**isoprostane** F2.alpha.-VI detection in human urine by gas chromatog./mass spectrometry)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

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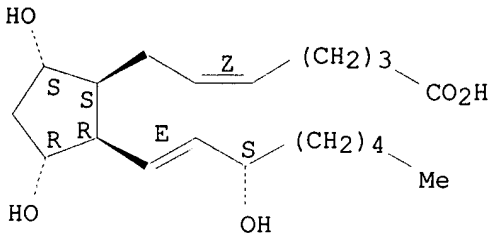
IT **27415-26-5**, 8-Iso-PGF2.alpha. **180469-63-0** **214894-56-1**
RL: **ANT (Analyte)**; BOC (Biological occurrence); **ANST (Analytical study)**; BIOL (Biological study); **OCCU (Occurrence)**
(8,12-iso- and 5-epi-8,12-iso-**isoprostane** F2.alpha.-VI detection in human urine by gas chromatog./mass spectrometry)

RN 27415-26-5 HCAPLUS

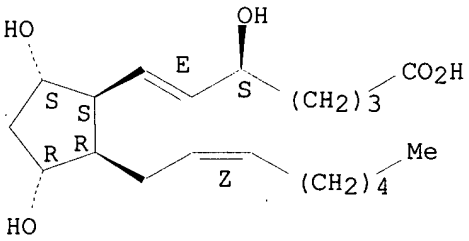
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



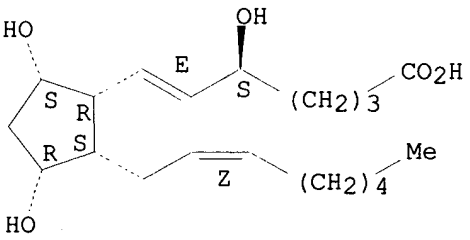
RN 180469-63-0 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 214894-56-1 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,9.alpha.,11.alpha.,12.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L64 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:618099 HCAPLUS
DN 129:310983
TI Total synthesis of 17,17,18,18-d4-**iPF2.alpha.**-**VI** and **quantification** of **iPF2.alpha**.-**VI** in human urine by gas chromatography/mass spectrometry
AU Adiyaman, Mustafa; Lawson, John A.; Khanapure, Subhash P.; **FitzGerald, Garret A.**; **Rokach, Joshua**
CS Claude Pepper Institute and Department of Chemistry, Florida Institute of Technology, Melbourne, FL, 32901-6975, USA
SO Anal. Biochem. (**1998**), 262(1), 45-56
CODEN: ANBCA2; ISSN: 0003-2697
PB Academic Press
DT Journal
LA English

CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 26

AB **Isoprostanes** are a new class of natural products formed in humans as a result of free-radical-catalyzed lipid peroxidn. of polyunsatd. fatty acids. These endogenous compds. are isomeric with biol. active prostaglandins and have great promise as markers of oxidant stress in vivo. **IPF2.alpha.-III** (previously 8-iso-PGF2.**alpha.**), an **isoprostane** from Class **III** (previously known as Class IV), has been used as an index of free-radical-induced oxidative stress. This **isoprostane** is also produced by the cyclooxygenase enzymes COX1 and COX2. The authors are proposing a new reliable index of oxidative stress based on **iPF2 .alpha.-VI** (previously **IPF2.alpha** .-I), a new Class **VI isoprostane** the authors recently discovered. The advantages of **iPF2.alpha.-VI** are that it is several fold more abundant in urine than **iPF2. alpha.-III**, hence allowing more accurate detns. Equally, the proximity of the C-5 OH function to the carboxylic acid allows the formation of the lactone 35 which is easier to purify from other iPs which cannot form such lactones. The authors have performed the first total synthesis of d4-**iPF2.alpha.-VI** by using two synthons, (3,3,4,4-d4)-hexylphosphonium bromide 23 prepd. from 5-hexynol and syn-anti-syn lactone 25 synthesized from D-glucose. The authors have developed two variants of a sensitive GC/MS assay using the synthetic d4-**iPF2.alpha.-VI** as an internal std. to det. the levels of endogenous **iPF2. alpha.-VI** in biol. fluids. Quantification of **iPF2.alpha.-VI** formed in vivo may be a more reliable index to assess oxidant stress in humans. (c) 1998 Academic Press.

ST **isoprostane** iPF2alphaVI urine analysis oxidative stress; d4 **iPF2alpha VI** prepn

IT Gas chromatography-mass spectrometry
Oxidative stress (biological)
Urine analysis
(total synthesis of 17,17,18,18-d4-**iPF2.alpha.- VI** and quantification of **iPF2.alpha.- VI** in human urine by gas chromatog.-mass spectrometry)

IT **180469-63-0, IPF2.alpha.-VI**
RL: **ANT (Analyte)**; RCT (Reactant); **ANST (Analytical study)**
(total synthesis of 17,17,18,18-d4-**iPF2.alpha.- VI** and quantification of **iPF2.alpha.- VI** in human urine by gas chromatog.-mass spectrometry)

IT 214977-79-4P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(total synthesis of 17,17,18,18-d4-**iPF2.alpha.- VI** and quantification of **iPF2.alpha.- VI** in human urine by gas chromatog.-mass spectrometry)

IT 70482-82-5P 70482-83-6P 70482-86-9P, 1-Hexan-3,3,4,4-d4-ol
70482-87-0P 70482-88-1P 214977-83-0P 214977-84-1P 214977-85-2P
214977-86-3P 214977-87-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of 17,17,18,18-d4-**iPF2.alpha.- VI** and quantification of **iPF2.alpha.- VI** in human urine by gas chromatog.-mass spectrometry)

IT 180300-33-8P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of 17,17,18,18-d4-**iPF2.alpha.- VI** and quantification of **iPF2.alpha.- VI** in human urine by gas chromatog.-mass spectrometry)

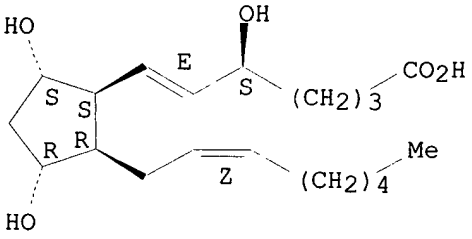
IT 110-87-2, 3,4-Dihydro-2H-pyran 603-35-0, Triphenylphosphine, reactions
1002-28-4, 3-Hexynol 104227-38-5 190390-52-4
RL: RCT (Reactant)

(total synthesis of 17,17,18,18-d4-**iPF2.alpha.-VI** and quantification of **iPF2.alpha.-VI** in human urine by gas chromatog.-mass spectrometry)

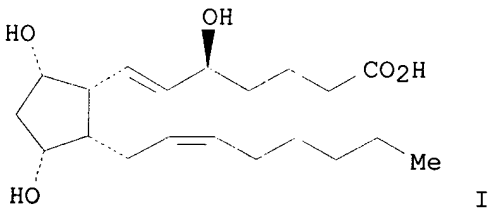
IT **180469-63-0, IPF2.alpha.-VI**
RL: **ANT (Analyte)**; RCT (Reactant); **ANST (Analytical study)**
(total synthesis of 17,17,18,18-d4-**iPF2.alpha.-VI** and quantification of **iPF2.alpha.-VI** in human urine by gas chromatog.-mass spectrometry)

RN 180469-63-0 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L64 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:603895 HCAPLUS
DN 129:316057
TI Syntheses and **identification** of the most abundant urinary type VI **isoprostanes**
AU Adiyaman, Mustafa; Lawson, John A.; **FitzGerald, Garret A.**; **Rokach, Joshua**
CS Claude Pepper Inst. Dep. Chem., Florida Inst. Technol., Melbourne, FL, 32901, USA
SO Tetrahedron Lett. (**1998**), 39(39), 7039-7042
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
CC 26-3 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 13
GI



I

AB The total synthesis of **8-12-iso-iPF2.alpha.-VI** (I) and its 5 epimer is described. With the aid of the synthetic materials these **isoprostanes** have been identified in and isolated from human urine.

ST urinary **isoprostane** prepn

IT Prostaglandins
RL: BOC (Biological occurrence); SPN (Synthetic preparation); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)

(syntheses and identification of most abundant urinary type VI **isoprostanes**)

IT 197151-20-5P **214894-56-1P**
RL: BOC (Biological occurrence); SPN (Synthetic preparation); BIOL (Biological study); **OCCU (Occurrence)**; PREP (Preparation)
(syntheses and identification of most abundant urinary type VI **isoprostanes**)

IT 4762-26-9 104227-38-5 214894-60-7
RL: RCT (Reactant)
(syntheses and identification of most abundant urinary type VI **isoprostanes**)

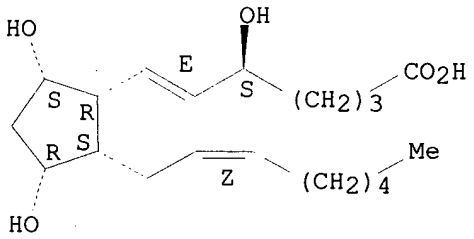
IT 214894-63-0P 214894-67-4P 214894-72-1P 214894-75-4P 214894-77-6P 214894-79-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(syntheses and identification of most abundant urinary type VI **isoprostanes**)

IT 214894-69-6P 214894-81-2P 214894-83-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(syntheses and identification of most abundant urinary type VI **isoprostanes**)

IT **214894-56-1P**
RL: BOC (Biological occurrence); SPN (Synthetic preparation); BIOL (Biological study); **OCCU (Occurrence)**; PREP (Preparation)
(syntheses and identification of most abundant urinary type VI **isoprostanes**)

RN 214894-56-1 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,9.alpha.,11.alpha.,12.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L64 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:369114 HCAPLUS
DN 129:144890
TI Cellular activation by thromboxane A2 and 8-epi-PGF2.alpha.
AU **Pratico, Domenico**; O'mahony, Dan; Lawson, John; Kinsella, Therese; **Fitzgerald, Garret A.**
CS Centre for Cardiovascular Science, Dept. of Medicine and Experimental Therapeutics, University College, Dublin, Ire.
SO Adv. Exp. Med. Biol. (**1997**), 400A(Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury 2, Pt. A), 229-233
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Publishing Corp.
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
AB A review with 14 refs. of the title subject. Thromboxane A2 is the predominant cyclooxygenase product of arachidonic acid in human platelets with potent vasoconstrictor and platelet activating properties. 8-Epi-PGF2.alpha., a free radical catalyzed PGF isomer, possesses vasoconstrictor and mitogenic properties. In contrast to TxA2, it induces platelet shape change, but not aggregation. Although the biol. effects of

this compd. are prevented by Tx antagonists, biochem. evidence has been presented that it acts preferentially via a related, but distinct receptor from that for TxA2.

ST **review** cellular activation thromboxane PGF2 isomer

IT Platelet (blood)
(cellular activation by thromboxane A2 and 8-epi-PGF2.alpha.)

IT Thromboxane receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(cellular activation by thromboxane A2 and 8-epi-PGF2.alpha.)

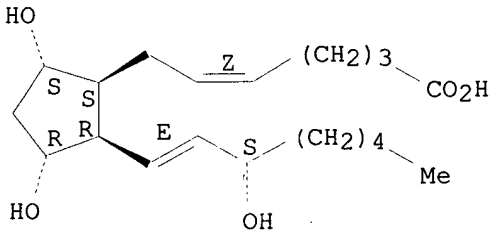
IT **27415-26-5**, 8-epi-PGF2.alpha. 57576-52-0, Thromboxane A2
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(cellular activation by thromboxane A2 and 8-epi-PGF2.alpha.)

IT **27415-26-5**, 8-epi-PGF2.alpha.
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(cellular activation by thromboxane A2 and 8-epi-PGF2.alpha.)

RN 27415-26-5 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L64 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:236003 HCAPLUS

DN 129:662

TI IPF2.alpha.-I: an **index** of lipid peroxidation in humans

AU **Pratico, Domenico**; Barry, Orla P.; Lawson, John A.; Adiyaman, Mustafa; Hwang, Seong-Woo; Khanapure, Subhash P.; Iuliano, Luigi; **Rokach, Joshua; Fitzgerald, Garret A.**

CS Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, 19104-6100, USA

SO Proc. Natl. Acad. Sci. U. S. A. (**1998**), 95(7), 3449-3454
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 4

AB **Isoprostanes** are prostaglandin isomers produced from arachidonic acid by a free radical-catalyzed mechanism. Urinary excretion of 8-iso-prostaglandin F2.alpha., an isomer of the PGG/H synthase (cyclooxygenase or COX) enzyme product, prostaglandin F2.alpha. (PGF2.alpha.), has exhibited promise as an index of oxidant stress in vivo. The authors have developed a quant. to measure **isoprostane** F2.alpha.-I, (IPF2.alpha.-I) a class I isomer (8-iso-PGF2.alpha. is class IV), using gas chromatog./mass spectrometry. IPF2.alpha.-I is severalfold as abundant in human urine as 8-iso-PGF2.alpha., with mean values of 737 pg/mg creatinine. Both **isoprostanes** are formed in a free radical-dependent manner in low d. lipoprotein oxidized by copper in vitro. However, IPF2.alpha.-I, unlike 8-iso-PGF2.alpha., is not formed in a COX-dependent manner by platelets activated by thrombin or collagen in

vitro. Similarly, COX inhibition in vivo has no effect on IPF2.alpha.-I. Neither serum IPF2.alpha.-I, an index of cellular capacity to generate the **isoprostane**, nor urinary excretion of IPF2.alpha.-I, an index of actual generation in vivo, is depressed by aspirin or indomethacin. In contrast, both serum thromboxane B2 and urinary excretion of its 11-dehydro metabolite are depressed by the COX inhibitors. Although serum 8-iso-PGF2.alpha. formation is substantially depressed by COX inhibitors, urinary excretion of the compd. is unaffected. Urinary IPF2.alpha.-I is elevated in cigarette smokers compared with controls (1525 vs. 740 pg/mg creatinine) and is highly correlated with urinary 8-iso-PGF2.alpha. (r = 0.9). Urinary IPF2.alpha.-I is a novel index of lipid peroxidn. in vivo, which can be measured with precision and sensitivity. It is an abundant F2-**isoprostane** formed in a free radical- but not COX-dependent manner. Although 8-iso-PGF2.alpha. may be formed as a minor product of COX, this pathway contributes trivially, if at all, to levels in urine. Urinary excretion of both **isoprostanes** is elevated in cigarette smokers.

ST **isoprostane** IPE2alphaI urine analysis lipid peroxidn; oxidative stress **isoprostane** urine cigarette smoke

IT Lipid peroxidation
Oxidative stress (biological)
Platelet (blood)
Tobacco smoke
Urine analysis
(IPF2.alpha.-I as index of lipid peroxidn. in humans)

IT Low-density lipoproteins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(IPF2.alpha.-I as index of lipid peroxidn. in humans)

IT Prostaglandins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IPF2.alpha.-I as index of lipid peroxidn. in humans)

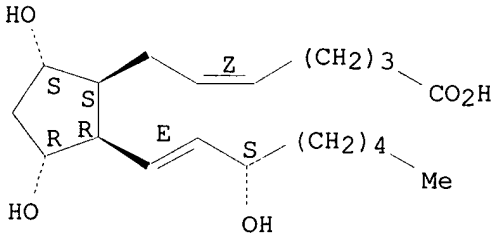
IT **27415-26-5**, 8-Iso-prostaglandin F2.alpha. **180469-63-0**
RL: **ANT (Analyte)**; BPR (Biological process); **ANST (Analytical study)**; BIOL (Biological study); PROC (Process)
(IPF2.alpha.-I as index of lipid peroxidn. in humans)

IT **39391-18-9**, Cyclooxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IPF2.alpha.-I as index of lipid peroxidn. in humans)

IT **27415-26-5**, 8-Iso-prostaglandin F2.alpha. **180469-63-0**
RL: **ANT (Analyte)**; BPR (Biological process); **ANST (Analytical study)**; BIOL (Biological study); PROC (Process)
(IPF2.alpha.-I as index of lipid peroxidn. in humans)

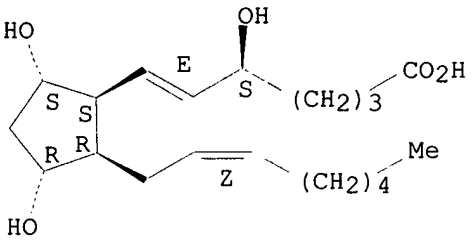
RN 27415-26-5 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 180469-63-0 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **39391-18-9**, Cyclooxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IPF2.alpha.-I as index of lipid peroxidn. in humans)
RN 39391-18-9 HCAPLUS
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)

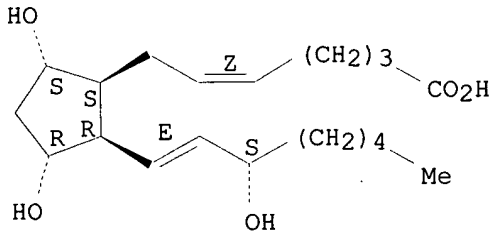
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L64 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:176669 HCAPLUS
DN 128:279019
TI The **isoprostanes**: a perspective
AU **Rokach, J.**; Khanapure, S. P.; Hwang, S.-W.; Adiyaman, M.; Lawson, J. A.; **FitzGerald, G. A.**
CS Claude Pepper Institute, Department Chemistry, Florida Institute Technology, Melbourne, FL, 32901-6975, USA
SO Prostaglandins (**1997**), 54(6), 823-851
CODEN: PRGLBA; ISSN: 0090-6980
PB Elsevier Science Inc.
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
Section cross-reference(s): 14
AB A review, with 99 refs. The **isoprostanes** are a new class of natural products produced in vivo by a non-enzymic free-radical-induced peroxidn. of polyunsatd. fatty acid. In the case of arachidonic acid, for example, four classes of **isoprostanes** can be produced. Because of the specific structural features distinguishing them from other free-radical-generated products, e.g., HETEs, etc., the **isoprostanes** can provide an exclusive and selective index for the oxidant component of several inflammatory and degenerative diseases. The possible mechanisms of formation of the individual **isoprostanes** is discussed in detail. Class III products, such as 8-iso-PGF2.alpha., and 8-iso-PGE2 have been shown to be vasoconstrictors and modulate platelet function. Several synthetic representatives from the four classes of arachidonic-acid-derived **isoprostanes** have already been prepd. by total synthesis. These synthetic stds. have been used for the identification and quantitation of these **isoprostanes** in biol. fluids using gas chromatog./mass spectrometry methodol.
ST **review isoprostane**
IT Eicosanoids
Leukotrienes
Prostaglandins
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative)

L64 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:24859 HCAPLUS
DN 128:87111
TI **Isoprostanes**: potential **markers** of oxidant stress in atherothrombotic disease
AU Patrono, Carlo; **Fitzgerald, Garret A.**
CS Center for Experimental Therapeutics and Department of Pharmacology,

University of Pennsylvania School of Medicine, Philadelphia, PA, 19104-6100, USA
SO Arterioscler., Thromb., Vasc. Biol. (**1997**), 17(11), 2309-2315
CODEN: ATVBFA; ISSN: 1079-5642
PB American Heart Association
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 4
AB A review, with 65 refs. **Isoprostanes** are emerging as a new class of biol. active products of arachidonic acid metab. of potential relevance to human vascular disease. Their formation in vivo seems to reflect primarily, if not exclusively, a nonenzymic process of lipid peroxidn. Enhanced urinary excretion of 8-iso-PGF2.alpha. has been described in assocn. with cardiac reperfusion injury and with cardiovascular risk factors, including cigarette smoking, diabetes mellitus, and hypercholesterolemia. Besides providing a likely noninvasive index of lipid peroxidn. in these settings, measurements of specific F2 **isoprostanes** in urine may provide a sensitive biochem. end point for dose-finding studies of natural and synthetic inhibitors of lipid peroxidn. Although the biol. effects of 8-iso-PGF2.alpha. in vitro suggest that it and other isoeicosanoids may modulate the functional consequences of lipid peroxidn., evidence that this is likely in vivo remains inadequate at this time.
ST **review** F2 **isoprostane** cardiovascular risk diagnosis
IT Cardiovascular diseases
Diabetes mellitus
Diagnosis
Hypercholesterolemia
Lipid peroxidation
Oxidative stress (biological)
Tobacco smoke
Urine analysis
Vascular diseases
(**isoprostanes** as potential markers of oxidant stress in atherothrombotic disease)
IT 551-11-1D, PGF2.alpha., isomers, F2 **isoprostanes**
27415-26-5, 8-Iso-PGF2.alpha.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**isoprostanes** as potential markers of oxidant stress in atherothrombotic disease)
IT **27415-26-5**, 8-Iso-PGF2.alpha.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**isoprostanes** as potential markers of oxidant stress in atherothrombotic disease)
RN 27415-26-5 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L64 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:764276 HCAPLUS

DN 128:58619
TI Cellular responses to eicosanoids: molecular biology of eicosanoid receptors
AU O'Mahony, Daniel J.; Kinsella, B. Therese; **Fitzgerald, Garret A.**
CS Elan Pharmaceutical Technologies, Trinity College, Dublin, Ire.
SO Princ. Med. Biol. (**1997**), Volume 8B, 385-405. Editor(s): Bittar, E. Edward; Bittar, Neville. Publisher: JAI Press, Greenwich, Conn. CODEN: 63ABAW
DT Conference; General Review
LA English
CC 6-0 (General Biochemistry)
AB A review with .apprx.55 refs. on arachidonic acid, prostaglandins, **isoprostanes**, and eicosanoid receptors including thromboxane A2 receptor and EP receptors.
ST **review** eicosanoid receptor arachidonate
IT Eicosanoids
Prostaglandins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cellular responses to eicosanoids, mol. biol. of eicosanoid receptors)
IT Receptors
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(eicosanoid; cellular responses to eicosanoids, mol. biol. of eicosanoid receptors)
IT 506-32-1, Arachidonic acid
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cellular responses to eicosanoids, mol. biol. of eicosanoid receptors)

L64 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:676782 HCAPLUS
DN 127:344749
TI Localization of distinct F2-**isoprostanes** in human atherosclerotic lesions
AU **Pratico, Domenico**; Iuliano, Luigi; Mauriello, Alessandro; Spagnoli, Luigi; Lawson, John A.; Maclouf, Jacques; Violi, Francesco; **Fitzgerald, Garret A.**
CS The Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO J. Clin. Invest. (**1997**), 100(8), 2028-2034
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
CC 14-5 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB F2-**Isoprostanes** are prostaglandin (PG) isomers formed in situ in cell membranes by peroxidn. of arachidonic acid. 8-Epi PGF2.alpha. and IPF2.alpha.-I are F2-**isoprostanes** produced in humans which circulate in plasma and are excreted in urine. Measurement of F2-**isoprostanes** may offer a sensitive, specific, and noninvasive method for measuring oxidant stress in clin. settings where reactive oxygen species are putatively involved. The authors detd. whether **isoprostanes** were present in human atherosclerotic lesions, where lipid peroxidn. is thought to occur in vivo. 8-Epi PGF2.alpha. ranged from 1.310-3.450 pmol/.mu.mol phospholipid in atherectomy specimens compared with 0.045-0.115 pmol/.mu.mol phospholipid in vascular tissue devoid of atherosclerosis. Corresponding values of IPF2.alpha.-I were 5.6-13.8 vs. 0.16-0.44 pmol/.mu.mol phospholipid. Levels of the two **isoprostanes** in vascular tissue were highly correlated (r = 0.80). Immunohistochem. studies confirmed that foam cells adjacent to the lipid necrotic core of the plaque were markedly pos. for 8-epi PGF2.alpha.. These cells were also reactive with anti-CD68, an epitope specific for human monocyte/macrophages. 8-Epi PGF2.alpha. immunoreactivity was also detected in cells pos. for anti-.alpha.-smooth muscle actin antibody, which specifically recognizes vascular smooth muscle cells. The authors' results indicate that 8-epi PGF2.alpha. and IPF2.alpha.-I, two distinct

F2-**isoprostanes** and markers of oxidative stress in vivo, are present in human atherosclerotic plaque. Quantitation of these chem. stable products of lipid peroxidn. in target tissues, as well as in biol. fluids, may aid in the rational development of antioxidant drugs in humans.

ST F2 **isoprostane** atherosclerotic lesion

IT Prostaglandins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(F2-**isoprostanes**; distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions)

IT Arterial diseases
(carotid, atherosclerotic lesion; distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions)

IT Carotid artery
(disease, atherosclerotic lesion; distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions)

IT Foam cell
Macrophage
Vascular smooth muscle
(distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions)

IT Lipid peroxidation
Oxidative stress (biological)
(distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions in relation to)

IT Reactive oxygen species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions in relation to)

IT Atherosclerosis
(lesion; distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions)

IT **27415-26-5**, 8 epi PGF2.alpha. **180469-63-0**, IPF2.alpha.-I
RL: BOC (Biological occurrence); BIOL (Biological study); **OCCU (Occurrence)**
(distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions)

IT **7782-44-7D**, Oxygen, reactive species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions in relation to)

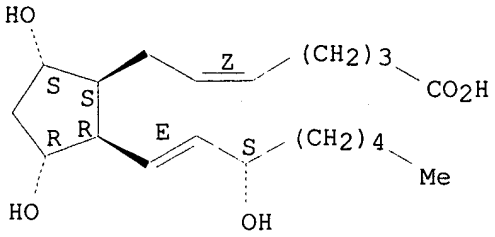
IT 506-32-1, Arachidonic acid
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(peroxidn. of lipid; distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions in relation to)

IT **27415-26-5**, 8 epi PGF2.alpha. **180469-63-0**, IPF2.alpha.-I
RL: BOC (Biological occurrence); BIOL (Biological study); **OCCU (Occurrence)**
(distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions)

RN 27415-26-5 HCAPLUS

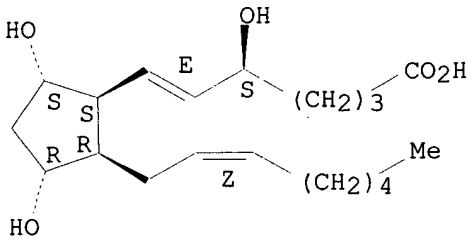
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 180469-63-0 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **7782-44-7D**, Oxygen, reactive species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(distinct F2-**isoprostanes** in monocyte/macrophage-derived foam cells and vascular smooth muscle cells in human atherosclerotic lesions in relation to)
RN 7782-44-7 HCAPLUS
CN Oxygen (8CI, 9CI) (CA INDEX NAME)

L64 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:413628 HCAPLUS
DN 127:147669
TI **Markers** of platelet activation and oxidant stress in atherothrombotic disease
AU **FitzGerald, Garret A.**; Tigges, Jessica; Barry, Patricia; Lawson, John A.
CS Center Experimental Therapeutics, University Pennsylvania, Philadelphia, PA, USA
SO Thromb. Haemostasis (**1997**), 78(1), 280-284
CODEN: THHADQ; ISSN: 0340-6245
PB Schattauer
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
AB A review is given with 68 refs. including the authors own work. Several new approaches to the study of platelet activation were developed. Logically, these should be combined with novel indexes of coagulant function to select rational targets for antithrombotic drugs. They may also be invaluable in dose-finding, which was a particular weakness in this area of drug development. While activation of platelets and the

coagulation cascade are virtually simultaneous events, markers of the atherosclerosis are also artificially segregated from those of, the complicating thrombotic process. Oxidant stress was implicated in both platelet activation and atherogenesis, yet the ability to study this system was so constrained that appropriate doses of antioxidant vitamins are unsure. Novel approaches to this problem promise the ability to study oxidative modification of proteins, lipids, and DNA in clin. studies.

ST **review** platelet **isoprostan** oxidative stress atherothrombosis

IT Oxidative stress (biological)
Platelet activation
Thrombosis
(markers of platelet activation and oxidant stress in atherothrombosis)

IT Prostaglandins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(markers of platelet activation and oxidant stress in atherothrombosis)

L64 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:409641 HCAPLUS
DN 127:93385
TI Novel **indices** of oxidant stress in cardiovascular disease: **specific analysis** of F2-**isoprostanes**
AU **Pratico, Domenico**; Reilly, Murdeach; Lawson, John A.; **FitzGerald, Garret A.**
CS 905 Stellar Chance Laboratories, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO Agents Actions Suppl. (**1997**), 48(Prostaglandins and Control of Vascular Smooth Muscle Cell Proliferation), 25-41
CODEN: AASUDJ; ISSN: 0379-0363
PB Birkhaeuser
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 9
AB A review with 61 refs. The development of methods to measure specific **isoprostanes** affords a unique opportunity to investigate both the role of oxidant stress as a mechanism of disease in vivo and to select rational doses of putative antioxidant drugs and vitamins for evaluation in human disease. The ability to measure these compds. directly in situ at the site of their formation, to immunolocalize them to target cells in atherosclerotic plaque and other tissues and to assess their biosynthesis non-invasively in urine promises to elucidate the role of lipid peroxidn. in cardiovascular disease.

ST **review isoprostane** oxidant stress cardiovascular disease

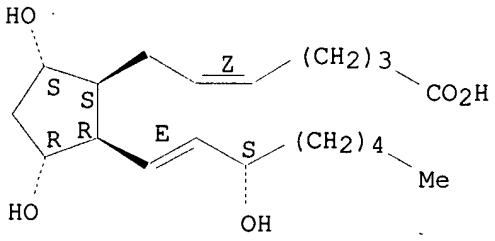
IT Prostaglandins
RL: ANT (Analyte); BOC (Biological occurrence); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(F2-**isoprostanes**; indexes of oxidant stress in human cardiovascular disease and specific anal. of F2-**isoprostanes** in relation to lipid peroxidn.)

IT Cardiovascular diseases
Lipid peroxidation
Oxidative stress (biological)
(indexes of oxidant stress in human cardiovascular disease and specific anal. of F2-**isoprostanes** in relation to lipid peroxidn.)

L64 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:398825 HCAPLUS
DN 127:76426
TI 8-Epi PGF2.alpha. generation during coronary reperfusion: a potential **quantitative marker** of oxidant stress in vivo
AU Delanty, N.; Reilly, M.P.; **Pratico, D.**; Lawson, J.A.; Mccarthy, J.F.; Wood, A.E.; Ohnishi, S.T.; Fitzgerald, D.J.; **Fitzgerald, G.A.**

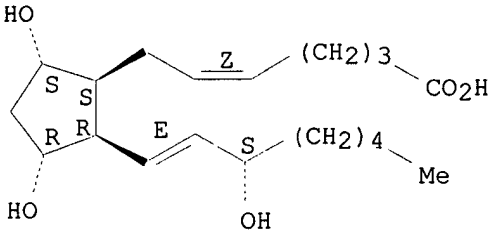
CS Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO Circulation (**1997**), 95(11), 2492-2499
CODEN: CIRCAZ; ISSN: 0009-7322
PB American Heart Association
DT Journal
LA English
CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 14
AB Myocardial reperfusion is believed to be assocd. with free radical injury. However, indexes of oxidative stress in vivo have been limited by their poor specificity and sensitivity. **Isoprostanes** are stable products of arachidonic acid formed in a nonenzymic, free radical-catalyzed manner. We have developed a sensitive and specific assay for one of these compds., 8-epi prostaglandin (PG) F2.alpha.. To address its utility as an index of oxidative stress during coronary reperfusion, we measured urinary levels by gas chromatog./mass spectrometry in a canine model of coronary thrombolysis, in patients with acute myocardial infarction treated with thrombolytic therapy, and in patients after elective coronary artery bypass surgery. Urinary 8-epi PGF2.alpha. was unchanged after circumflex artery occlusion in a canine model of coronary thrombolysis (437.2.+-.56.4 vs. 432.7.+-.55.2 pmol/mmol creatinine) but increased significantly immediately after reperfusion (553.8.+-.64.7 pmol/mmol). Urinary levels were increased in patients with acute myocardial infarction given lytic therapy (265.8.+-.40.8 pmol/mmol) compared with age-matched control subjects (91.5.+-.11.8 pmol/mmol) and patients with stable coronary disease (95.7.+-.6.3 pmol/mmol). Preoperative levels rose from 113.2.+-.11.8 to 248.2.+-.86.3 pmol/mmol at 30 min into revascularization to 332.2.+-.82.6 pmol/mmol by 15 min after global myocardial reperfusion (P.05) and dropped to 181.2.+-.50.4 pmol/mmol at 30 min and 120.2.+-.9.9 pmol/mmol at 24 h after bypass surgery. Corresponding changes in spin adduct formation, found with ESR, were noted in 2 patients. These data support the hypothesis that free radical generation occurs during myocardial reperfusion. Measurement of **isoprostane** prodn. may serve as a noninvasive index of oxidative stress.
ST epiPGF2 coronary reperfusion oxidant stress; **isoprostane** free radical reperfusion injury heart
IT Heart
Surgery
(aortocoronary bypass surgery; epiPGF2.alpha. generation during coronary reperfusion as marker of oxidant stress)
IT Fibrinolysis
Myocardial infarction
Oxidative stress (biological)
Reperfusion injury
Urine
(epiPGF2.alpha. generation during coronary reperfusion as marker of oxidant stress)
IT Reactive oxygen species
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(epiPGF2.alpha. generation during coronary reperfusion as marker of oxidant stress)
IT **27415-26-5**
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(epiPGF2.alpha. generation during coronary reperfusion as marker of oxidant stress)
IT **27415-26-5**
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(epiPGF2.alpha. generation during coronary reperfusion as marker of oxidant stress)
RN 27415-26-5 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L64 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:365560 HCAPLUS
DN 127:79348
TI Urinary 8-Epi PGF2.alpha.: an **index** of oxidant stress in vivo
AU Reilly, M. P.; Barry, P.; Lawson, J. A.; **Fitzgerald, G.**
CS The Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO Fibrinolysis Proteolysis (**1997**), 11(Suppl. 1, Third International Fibrinogen Symposium: Hemostasis, Inflammation and Cardiovascular Disease, 1996), 81-84
CODEN: FBPRFP
PB Churchill Livingstone
DT Journal; General Review
LA English
CC 14-0 (Mammalian Pathological Biochemistry)
AB A review, with 20 refs. Isoeicosanoids are free radical catalyzed products of arachidonic acid. To explore their biol. and potential utility as indexes of oxidant stress, the authors have focused upon one isomer, 8-epi PGF2.alpha.. Excretion of this compd. is increased in syndromes putatively assocd. with oxidant stress, including poisoning with paraquat and paracetemol, cigarette smoking, alc. intake, diabetic ketosis, ARDS, and syndromes of vascular reperfusion. 8-Epi may also be formed by cyclooxygenase (COX)-1 in platelets and by COX-2 in monocytes, although these pathways are minor contributors to overall biosynthesis. Monocytes also retain the capacity to form 8-epi as an **isoprostane** when stimulated with zymosan in the presence of LDL. Identification of 8-epi in human plaque and elevated excretion in hypercholesterolemia suggest its utility in exploring the role of oxidant stress in atherosclerosis. 8-Epi may also amplify the affects of platelet agonists in the local microenvironment in syndromes where platelet activation and oxidant injury coincide.
ST **review** PGF2alpha deriv urine oxidant stress
IT Atherosclerosis
Oxidative stress (biological)
Urine
(urinary epi-PGF2.alpha. as index of oxidant stress in vivo)
IT **27415-26-5**, 8-Epi-PGF2.alpha.
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urinary epi-PGF2.alpha. as index of oxidant stress in vivo)
IT **27415-26-5**, 8-Epi-PGF2.alpha.
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urinary epi-PGF2.alpha. as index of oxidant stress in vivo)
RN 27415-26-5 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L64 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:337821 HCAPLUS
DN 127:29140
TI **Isoprostanes** and antioxidant therapy in human diseases
AU Meagher, Emma A.; **Fitzgerald, Garret A.**
CS The University of Pennsylvania, Philadelphia, PA, USA
SO Fundam. Clin. Cardiol. (**1997**), 29(Endothelium in Clinical Practice), 413-438
CODEN: FCCAEH; ISSN: 1067-5264
PB Dekker
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
Section cross-reference(s): 1
AB A review, with 117 refs., which discusses: assessment of oxidant stress; antioxidant drugs; and antioxidant drugs and clin. trials.
ST **review isoprostane** antioxidant disease
IT Antioxidants (pharmaceutical)
Diseases (animal)
(**isoprostanes** and antioxidant therapy in human diseases)
IT Prostaglandins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**isoprostanes** and antioxidant therapy in human diseases)

L64 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:473623 HCAPLUS
DN 125:158765
TI 8-Epi PGF2.alpha.: **Specific analysis** of an isoeicosanoid as an **index** of oxidant stress in vivo
AU Delanty, N.; Reilly, M.; **Pratico, D.**; Fitzgerald, D. J.; Lawson, J. A.; **Fitzgerald, G. A.**
CS Center Experimental Therapeutics, University Pennsylvania, Philadelphia, PA, 19104, USA
SO Br. J. Clin. Pharmacol. (**1996**), 42(1), 15-19
CODEN: BCPHBM; ISSN: 0306-5251
DT Journal
LA English
CC 2-1 (Mammalian Hormones)
AB Excessive free radical generation is thought to contribute to tissue injury in a broad spectrum of diseases. A particular constraint in addressing this hypothesis has been the inability to assess free radical generation in vivo and the lack of information on drugs or vitamins which act as effective antioxidants in vivo. Traditional approaches have relied upon measures of substrate oxidizability or spin trapping of free radical adducts ex vivo. It is unknown how these measurements might relate, in a quant. fashion, to the generation of reactive oxygen species in vivo. Isoeicosanoids are free radical catalyzed products of arachidonic acid. One of these compds., 8-epiprostaglandin F2.alpha. (8-epi PGF2.alpha.) exhibits biol. activity and may function as an autacoid. Specific anal. of this 8-epi PGF2.alpha. isomer indicates that it is elevated in certain syndromes thought to be assocd. with oxidant stress. These include vascular reperfusion, paracetamol poisoning and liver cirrhosis.

Apparently healthy individuals who smoke cigarettes or consume alc. exhibit dose dependent increments in excretion of 8-epi PGF2.alpha.. Excretion is depressed by antioxidant vitamins, although not by the nonspecific cyclooxygenase (COX) inhibitor, aspirin, even though 8-epi PGF2.alpha. may be formed by either COX-1 or COX-2. Specific anal. of this and other isoeicosanoids may afford an opportunity to evaluate the effects of antioxidant interventions in human diseases characterized by excessive lipid peroxidn. in vivo.

ST epi PGF2 urine oxidant stress index

IT Cirrhosis
Oxidative stress, biological
Tobacco smoke and smoking
Urine analysis
(epi-PGF2.alpha. detn. in urine as index of oxidant stress in vivo)

IT Radicals, biological studies
Reactive oxygen species
RL: ANT (Analyte); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(epi-PGF2.alpha. detn. in urine as index of oxidant stress in vivo)

IT Perfusion
(re-, epi-PGF2.alpha. detn. in urine as index of oxidant stress in vivo)

IT 64-17-5, Ethanol, biological studies 103-90-2, Paracetamol 4685-14-7, Paraquat
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(epi-PGF2.alpha. detn. in urine as index of oxidant stress in vivo)

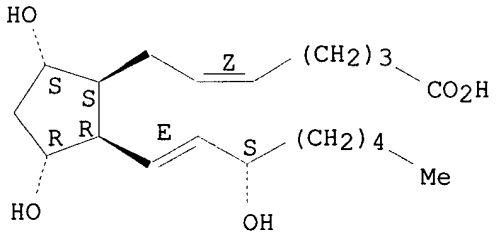
IT **27415-26-5**, 8-Epi-PGF2.alpha.
RL: MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(epi-PGF2.alpha. detn. in urine as index of oxidant stress in vivo)

IT **27415-26-5**, 8-Epi-PGF2.alpha.
RL: MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(epi-PGF2.alpha. detn. in urine as index of oxidant stress in vivo)

RN 27415-26-5 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L64 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:436542 HCAPLUS

DN 125:167609

TI Total synthesis of a novel **isoprostane** IPF2.alpha.-I and its **identification** in biological fluids

AU Adiyaman, Mustafa; Lawson, John A.; Hwang, Seong-Woo; Khanapure, Subhash P.; **FitzGerald, Garret A.**; **Rokach, Joshua**

CS Claude Pepper Inst., Florida Inst. Technol., Melbourne, FL, 32901, USA

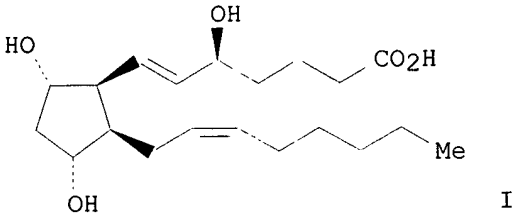
SO Tetrahedron Lett. (**1996**), 37(28), 4849-4852
CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA English

CC 26-3 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 33
OS CASREACT 125:167609
GI



I

AB The first total synthesis of IPF2.alpha.-I (I) is described using D-glucose as starting material. This novel **isoprostane** has been used to establish its presence in human urine.

ST glucose conversion IPF2alphaI; prostane IPF2alphaI prepn occurrence biol fluids

IT Asymmetric synthesis and induction
(total synthesis of novel **isoprostane** IPF2.alpha.-I and its identification in biol. fluids)

IT **180469-63-0P**
RL: BOC (Biological occurrence); SPN (Synthetic preparation); BIOL (Biological study); **OCCU (Occurrence)**; PREP (Preparation)
(total synthesis of novel **isoprostane** IPF2.alpha.-I and its identification in biol. fluids)

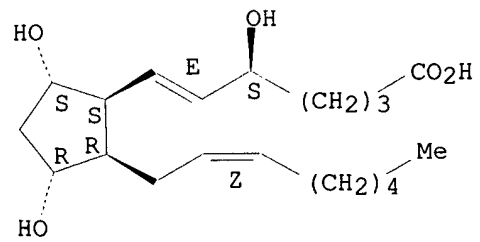
IT 50-99-7, D-Glucose, reactions 582-52-5, 1,2:5,6-Di-O-isopropylidene-.alpha.-D-glucofuranose 1501-26-4, Methyl 5-chloro-5-oxopentanoate 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 4762-26-9, Hexyltriphenylphosphonium bromide 16667-96-2
RL: RCT (Reactant)
(total synthesis of novel **isoprostane** IPF2.alpha.-I and its identification in biol. fluids)

IT 4494-96-6P 4613-62-1P 76700-85-1P 104227-38-5P 155518-70-0P 159812-84-7P 180300-29-2P 180300-30-5P 180300-31-6P 180300-32-7P 180300-33-8P 180300-34-9P 180300-35-0P 180300-36-1P 180469-61-8P 180469-62-9P 180469-64-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of novel **isoprostane** IPF2.alpha.-I and its identification in biol. fluids)

IT **180469-63-0P**
RL: BOC (Biological occurrence); SPN (Synthetic preparation); BIOL (Biological study); **OCCU (Occurrence)**; PREP (Preparation)
(total synthesis of novel **isoprostane** IPF2.alpha.-I and its identification in biol. fluids)

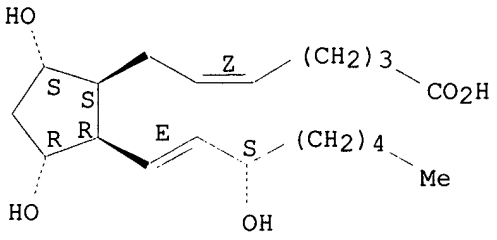
RN 180469-63-0 HCAPLUS
CN Prosta-6,14-dien-1-oic acid, 5,9,11-trihydroxy-, (5S,6E,8.beta.,9.alpha.,11.alpha.,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L64 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:886471 HCAPLUS
DN 123:276205
TI Immunological characterization of urinary 8-epi-prostaglandin F2.alpha. excretion in man
AU Wang, Zhaoyue; Ciabattoni, Giovanni; Creminon, Christophe; Lawson, John; **Fitzgerald, Garret A.**; Patrono, Carlo; Maclouf, Jacques
CS U348 INSERM, I.F.R. Vaisseaux-Lariboisiere Hopital Lariboisiere, Paris, 75475, Fr.
SO J. Pharmacol. Exp. Ther. (**1995**), 275(1), 94-100
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
CC 2-1 (Mammalian Hormones)
AB F2-**isoprostanes** are prostaglandin (PG) F2-like compds. that are formed in vivo directly by free radical-catalyzed lipid peroxidn. One of the compds. that can be produced in abundance by such mechanism is 8-epi-PGF2.alpha., a potent vasoconstrictor. We have developed an enzyme immunoassay and a RIA for measuring urinary concns. of 8-epi-PGF2.alpha. by raising antibodies against this compd. The antisera presented high titers (>1/300,000) and provided highly sensitive assays (IC50, 8 and 24 pg/mL, for EIA and RIA, resp.); cross-reactivity with other PG was negligible. The interassay reproducibility of EIA was assessed by measuring the same urine stored frozen in aliquots after solid phase extn. and thin-layer chromatog. (17%). Measurements of urinary 8-epi-PGF2.alpha. by immunoassays were validated using different antisera and by comparison with gas chromatog./mass spectrometry. Healthy volunteers excreted 25 ng of 8-epi-PGF2.alpha./mmol creatinine, with no circadian variation over three consecutive 8-h collection periods; preliminary results showed that excretion increased as a function of age. Urinary excretion of 8-epi-PGF2.alpha. was unchanged by treatment with two nonsteroidal antiinflammatory drugs, ibuprofen at 1.2 g/day for 4 days or aspirin as a single administration of 1 g. In contrast, the urinary excretion of 11-dehydro-thromboxane B2, a platelet cyclooxygenase-derived metabolite, was reduced by more than 80% after aspirin administration. Anal. of serum revealed a small (0.1% of thromboxane B2) but consistent prodn. of 8-epi-PGF2.alpha. by a cyclooxygenase-dependent mechanism totally suppressed after administration of aspirin to the same subjects. Monitoring of this compd. in urine or plasma may turn to be a useful index of in vivo lipid peroxidn.
ST urine epiprostaglandin F2 immunoassay
IT Urine
(age-dependent urinary excretion of epiprostaglandin F2.alpha. in man)
IT Senescence
Urine analysis
(epiprostaglandin F2.alpha. detn. in urine of man by immunoassay and effect on age)
IT **27415-26-5**, 8-epi-Prostaglandin F2.alpha.
RL: **ANT (Analyte)**; BPR (Biological process); **ANST (Analytical study)**; BIOL (Biological study); PROC (Process)
(epiprostaglandin F2.alpha. detn. in urine of man by immunoassay and effect on age)
IT **27415-26-5**, 8-epi-Prostaglandin F2.alpha.
RL: **ANT (Analyte)**; BPR (Biological process); **ANST (Analytical study)**; BIOL (Biological study); PROC (Process)
(epiprostaglandin F2.alpha. detn. in urine of man by immunoassay and effect on age)
RN 27415-26-5 HCAPLUS
CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,8.beta.,9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



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L82 ANSWER 1 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:523317 BIOSIS
DN PREV199900523317
TI A newly-discovered **isoprostane** is a marker of oxidative stress in LPS-mediated inflammation in humans.
AU Mardini, Issam A. (1); Lawson, John A. (1); **Rokach, Joshua A.**; Adiyaman, Mustafa; Hwang, Seong-Woo; Khanapure, Subhash P.; Schumacher, Kathlyn J. (1); **Fitzgerald, Garret A. (1)**
CS (1) Univ. Pennsylvania, Philadelphia, PA USA
SO Circulation, (**Oct. 27, 1998**) Vol. 98, No. 17 SUPPL., pp. I7.
Meeting Info.: **71st Scientific Sessions of the American Heart Association** Dallas, Texas, USA November 8-11, 1998 The American Heart Association
. ISSN: 0009-7322.
DT **Conference**
LA English
CC Cardiovascular System - General; Methods *14501
Biophysics - General Biophysical Techniques *10504
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Biochemical Studies - General *10060
IT Major Concepts
Cardiovascular System (Transport and Circulation)
IT Chemicals & Biochemicals
F-2-**isoprostane**: newly discovered, oxidative stress marker
IT Methods & Equipment
GC/MS: analytical method
IT Miscellaneous Descriptors
inflammation: LPS-mediated; oxidative stress; **Meeting** Abstract

L82 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:17496 BIOSIS
DN PREV199800017496
TI Urinary extension of IPF2alpha-1 and 8-epi PGF2alpha: Specific analysis of

distinct F2 **isoprostanes** as noninvasive indices of oxidant stress in vivo.
AU **Pratico, Domenico (1)**; Barry, Orla P. (1); Lawson, John A. (1); **Rokach, Joshua; Fitzgerald, Garret A.**
CS (1) Univ. Pa., Philadelphia, PA USA
SO Circulation, (**10/21/97, 1997**) Vol. 96, No. 8 SUPPL., pp. I417. Meeting Info.: **70th Scientific Sessions of the American Heart Association** Orlando, Florida, USA November 9-12, 1997 ISSN: 0009-7322.
DT **Conference**
LA English
CC Metabolism - Lipids *13006
Biophysics - Bioenergetics: Electron Transport and Oxidative Phosphorylation *10510
Physiology, General and Miscellaneous - Stress *12008
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
monocyte: blood and lymphatics, immune system
IT Chemicals & Biochemicals
arachidonic acid; prostaglandin F-2 **isoprostane**: oxidant stress indicator; prostaglandin F-2-alpha: urinary excretion; thromboxane B-2; 8-epi-prostaglandin F-2-alpha: urinary excretion
IT Miscellaneous Descriptors
oxidant stress; **Meeting** Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 551-11-1 (PROSTAGLANDIN F-2-ALPHA)
54397-85-2 (THROMBOXANE B-2)
506-32-1 (ARACHIDONIC ACID)

L82 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:241470 BIOSIS
DN PREV199799540673
TI Brain **isoprostane** levels are elevated in Alzheimer's disease.
AU **Pratico, Domenico**; Lee, Virginia M.-Y.; **Trojanowski, John Q.**; **Fitzgerald, Garret A.**
CS Cent. Exp. Therapeutics, Univ. Pa. Sch. Med., Philadelphia, PA USA
SO Journal of Investigative Medicine, (1997) Vol. 45, No. 3, pp. 238A. Meeting Info.: **Annual Meeting of the Association of American Physicians, the American Society for Clinical Investigation, and the American Federation for Medical Research: Biomedicine '97 Medical Research from Bench to Bedside** Washington, D.C., USA April 25-27, 1997 ISSN: 1081-5589.
DT **Conference**; Abstract; **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemistry - Gases *10012
Biochemical Studies - Sterols and Steroids 10067
Endocrine System - General *17002
Nervous System - Pathology *20506
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Endocrine System (Chemical

Coordination and Homeostasis); Neurology (Human Medicine, Medical Sciences)
IT Chemicals & Biochemicals
OXYGEN FREE RADICALS
IT Miscellaneous Descriptors
BRAIN; ENDOCRINE SYSTEM; **ISOPROSTANE** F-2ALPHA; NERVOUS SYSTEM; OXIDATIVE STRESS; OXYGEN FREE RADICALS; PATIENT; 8-EPI-PROSTAGLANDIN-F-2ALPHA
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 11062-77-4 (OXYGEN FREE RADICALS)

L82 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:241302 BIOSIS
DN PREV199799540505
TI **Isoprostane** biosynthesis: Close correlation of two distinct F2 **isoprostanes** in syndromes of oxidant stress.
AU Reilly, Muredach P.; **Pratico, Domenico**; Rokach, Joseph; Lawson, John; **Fitzgerald, Garret A.**
CS Univ. Pa., Philadelphia, PA USA
SO Journal of Investigative Medicine, (1997) Vol. 45, No. 3, pp. 210A.
Meeting Info.: **Annual Meeting of the Association of American Physicians, the American Society for Clinical Investigation, and the American Federation for Medical Research: Biomedicine '97 Medical Research from Bench to Bedside** Washington, D.C., USA April 25-27, 1997
ISSN: 1081-5589.
DT **Conference**; Abstract; **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Clinical Biochemistry; General Methods and Applications *10006
Biophysics - Molecular Properties and Macromolecules *10506
Metabolism - Lipids *13006
Metabolism - Sterols and Steroids *13008
Metabolism - Metabolic Disorders *13020
Endocrine System - General *17002
Toxicology - General; Methods and Experimental *22501
Developmental Biology - Embryology - Pathological *25503
IT Major Concepts
Biochemistry and Molecular Biophysics; Clinical Chemistry (Allied Medical Sciences); Development; Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Toxicology
IT Chemicals & Biochemicals
PROSTAGLANDIN F2-ALPHA
IT Miscellaneous Descriptors
ACUTE MYOCARDIAL INFARCTION; CARDIOVASCULAR MEDICINE; CIGARETTE SMOKING; CLINICAL CHEMISTRY; FAMILIAL HOMOZYGOUS HYPERCHOLESTEROLEMIA; F2 **ISOPROSTANES**; GENETIC DISEASE; HEART DISEASE; METABOLIC DISEASE; OXIDANT STRESS; VASCULAR DISEASE; 8-EPI PROSTAGLANDIN F2-ALPHA
RN 551-11-1 (PROSTAGLANDIN F2-ALPHA)

L82 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:3661 BIOSIS
DN PREV199799302864
TI Monocytes in human atherosclerotic plaque contain high levels of 8-epi PGF-2alpha: An index of oxidative stress in vivo.
AU **Pratico, Domenico (1)**; Iuliano, Luigi; Spagnoli, Luigi; Mauriello, A.; Maclouf, Jacques; Violi, Francesco; **Fitzgerald, Garrett A.**
CS (1) Univ. Pennsylvania, Philadelphia, PA USA
SO Circulation, (1996) Vol. 94, No. 8 SUPPL., pp. I277.
Meeting Info.: **69th Scientific Sessions of the American Heart**

Association New Orleans, Louisiana, USA November 10-13, 1996
ISSN: 0009-7322.
DT **Conference**; Abstract
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General *10060
Pathology, General and Miscellaneous - General *12502
Metabolism - General Metabolism; Metabolic Pathways *13002
Cardiovascular System - General; Methods *14501
IT Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Metabolism; Pathology
IT Chemicals & Biochemicals
PROSTAGLANDIN F-2 ALPHA
IT Miscellaneous Descriptors
ATHEROSCLEROSIS; BLOOD AND LYMPHATICS; CARDIOVASCULAR SYSTEM; **ISOPROSTANE**; LIPID PEROXIDATION; MONOCYTE; OXIDATIVE STRESS; OXIDATIVE STRESS INDEX; VASCULAR DISEASE; 8-EPI PGF-2 ALPHA; 8-EPI PROSTAGLANDIN F-2 ALPHA
RN 551-11-1 (PROSTAGLANDIN F-2 ALPHA)

L82 ANSWER 6 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:3305 BIOSIS
DN PREV199799302508
TI Elevated urinary 8-epi-PGF2-alpha, an in vivo index of oxidant stress in pregnancy-induced hypertension.
AU Robinson, Charlah A.; Lawson, John; Morgan, Mark A.; **Fitzgerald, Garret A.**
CS Univ. Pennsylvania Med. Center, Philadelphia, PA USA
SO Circulation, (1996) Vol. 94, No. 8 SUPPL., pp. I215-I216.
Meeting Info.: **69th Scientific Sessions of the American Heart Association** New Orleans, Louisiana, USA November 10-13, 1996
ISSN: 0009-7322.
DT **Conference**; Abstract
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Physiology, General and Miscellaneous - Stress *12008
Metabolism - General Metabolism; Metabolic Pathways *13002
Metabolism - Lipids *13006
Cardiovascular System - Blood Vessel Pathology *14508
Reproductive System - Pathology *16506
Endocrine System - General *17002
BC Hominidae *86215
IT Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Physiology; Reproductive System (Reproduction)
IT Chemicals & Biochemicals
PROSTAGLANDIN F2-ALPHA
IT Miscellaneous Descriptors
CARDIOVASCULAR MEDICINE; ENDOCRINE SYSTEM; FEMALE; F2-**ISOPROSTANE**; HEMODYNAMICS; OBSTETRICS; OXIDANT STRESS; PATIENT; PREECLAMPSIA; PREGNANCY-INDUCED HYPERTENSION; PROSTAGLANDIN F2-ALPHA; REPRODUCTIVE SYSTEM DISEASE/FEMALE; VASCULAR DISEASE
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 551-11-1 (PROSTAGLANDIN F2-ALPHA)

L82 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:449047 BIOSIS

DN PREV199699171403
TI Total synthesis of IPF-2alpha-I: A major urinary **isoprostane.**
AU Adiyaman, M. (1); Lawson, J. A.; Hwang, S. W. (1); Khanapure, S. P. (1); **Fitzgerald, G. A.; Rokach, J. (1)**
CS (1) Claude Pepper Inst., Dep. Chem., Florida Inst. of Technol., 150 W. University Blvd., Melbourne, FL 32901 USA
SO Abstracts of Papers American Chemical Society, (1996) Vol. 212, No. 1-2, pp. ORGN 66.
Meeting Info.: **212th American Chemical Society National Meeting** Orlando, Florida, USA August 25-29, 1996
ISSN: 0065-7727.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Methods - General *10050
Biochemical Methods - Lipids *10056
Biochemical Studies - General *10060
Biochemical Studies - Lipids *10066
Biophysics - Molecular Properties and Macromolecules *10506
Urinary System and External Secretions - Physiology and Biochemistry *15504
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques; Urinary System (Chemical Coordination and Homeostasis)
IT Chemicals & Biochemicals
IPF-2ALPHA-I
IT Miscellaneous Descriptors
MEETING ABSTRACT; NATURAL PRODUCT; SYNTHETIC METHOD
RN **180469-63-0** (IPF-2ALPHA-I)

L82 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:308268 BIOSIS
DN PREV199699030624
TI **Isoprostanes**-indices of oxidant stress.
AU **Fitzgerald, G. A.**
CS Univ. Pa. Sch. Med., Philadelphia, PA 19104 USA
SO FASEB Journal, (1996) Vol. 10, No. 6, pp. A1138.
Meeting Info.: **Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists** New Orleans, Louisiana, USA June 2-6, 1996
ISSN: 0892-6638.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Human 02508
Biochemistry - Gases *10012
Biochemical Studies - General 10060
Biochemical Studies - Lipids 10066
Biochemical Studies - Sterols and Steroids 10067
Biochemical Studies - Carbohydrates 10068
Biophysics - Molecular Properties and Macromolecules 10506
Metabolism - Carbohydrates 13004
Metabolism - Sterols and Steroids 13008
Metabolism - Metabolic Disorders *13020
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Respiratory System - Pathology *16006
Endocrine System - General *17002
Endocrine System - Pancreas *17008
Toxicology - General; Methods and Experimental *22501
BC Hominidae *86215

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Pulmonary Medicine (Human Medicine, Medical Sciences); Toxicology
IT Chemicals & Biochemicals
ARACHIDONIC ACID; PROSTAGLANDIN F2ALPHA; PARAQUAT; PARACETAMOL; ALCOHOL
IT Miscellaneous Descriptors
ADULT RESPIRATORY DISTRESS SYNDROME; ALCOHOL INTAKE; ARACHIDONIC ACID; ATHEROSCLEROSIS; DIABETIC KETOSIS; HYPERCHOLESTEROLEMIA; **MEETING** ABSTRACT; MONOCYTE; PARACETAMOL; PARAQUAT; PLATELET; POISONING; SMOKING; VASCULAR PERFUSION; 8-EPI PROSTAGLANDIN F2ALPHA
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 506-32-1 (ARACHIDONIC ACID)
551-11-1 (PROSTAGLANDIN F2ALPHA)
4685-14-7 (PARAQUAT)
103-90-2 (PARACETAMOL)
64-17-5 (ALCOHOL)

L82 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:11780 BIOSIS
DN PREV199698583915
TI Prostaglandin G/H synthase dependent formation of the **isoprostane**, 8-epi PGF-2-alpha.
AU **Pratico, Domenico; Fitzgerald, Garret A.**
CS Univ. Pa., Philadelphia, PA USA
SO Circulation, (1995) Vol. 92, No. 8 SUPPL., pp. I303.
Meeting Info.: **68th Scientific Session of the American Heart Association** Anaheim, California, USA November 13-16, 1995
ISSN: 0009-7322.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemistry - Gases 10012
Biochemical Studies - Lipids 10066
Enzymes - Physiological Studies *10808
Physiology, General and Miscellaneous - Stress 12008
Metabolism - Lipids *13006
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Endocrine System - General *17002
BC Hominidae *86215
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Metabolism
IT Chemicals & Biochemicals
PROSTAGLANDIN F2-ALPHA; ARACHIDONIC ACID
IT Miscellaneous Descriptors
ARACHIDONIC ACID; **MEETING** ABSTRACT; METABOLISM; OXIDATIVE STRESS; PLATELET; PROSTAGLANDIN F2-ALPHA
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 551-11-1 (PROSTAGLANDIN F2-ALPHA)
506-32-1 (ARACHIDONIC ACID)

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    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<


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L90  ANSWER 1 OF 1  WPIX   COPYRIGHT 2002   DERWENT INFORMATION LTD
AN   2000-412349 [35]   WPIX
DNN  N2000-308183       DNC C2000-125076
TI   Measuring level of lipid peroxidation for diagnosing oxidant stress
     syndrome/disease such as Alzheimer's disease, involves comparing level of
     isoprostane molecule marker in samples from normal and diseased
     mammals.
DC   B04 D16 S03
IN   FITZGERALD, G A; PRATICO, D; ROKACH, J;
     TROJANOWSKI, J Q
PA   (FLOR-N) FLORIDA INST TECHNOLOGY; (UYPE-N) UNIV PENNSYLVANIA
CYC  23
PI   WO 2000032805 A1 20000608 (200035)* EN   58p    C12P031-00
        RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
         W: AU CA JP US
     AU 2000031083 A  20000619 (200044)             C12P031-00
     EP 1135519    A1 20010926 (200157)  EN         C12P031-00
         R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT  WO 2000032805 A1 WO 1999-US28583 19991202; AU 2000031083 A AU 2000-31083
     19991202; EP 1135519 A1 EP 1999-965096 19991202, WO 1999-US28583 19991202
FDT  AU 2000031083 A Based on WO 200032805; EP 1135519 A1 Based on WO 200032805
PRAI US 1998-110569P  19981202
IC   ICM  C12P031-00
     ICS  C12Q001-26; G01N033-53
AB   WO 200032805 A UPAB: 20000725
     NOVELTY - Measuring level of lipid peroxidation in a mammal suspected of
     having an oxidant stress syndrome/disease (OS) involves comparing the
     level of isoprostane molecule marker (I) in samples (Ia) and
     (Ib) obtained from diseased and normal mammals respectively. An elevated
     level of (I) in (Ia) relative to the level in (Ib), indicates the presence
     of OS.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following:
          (1) identifying a compound (II) useful for the treatment of
     Alzheimer's disease (AD), involving comparing the level of (I) prior to
     and after administration of (II) in a mammal, where (II) which reduces the
     level of (I), is identified as the compound useful for treatment of AD;
          (2) determining the optimal concentration or dosage frequency of (II)
     involving monitoring the level of (I) in a series of mammals administered
     with (II), at a series of concentration or dosage frequencies not toxic to
     the mammal, which results in maximal reduction of the level of (I), is the
     optimal concentration or optimal dosage frequency; and
```

(3) a kit for measuring level of (I) comprising:
(i) sample container for carrying a tissue or body fluid sample;
(ii) a solution for extraction of (I);
(iii) a negative and positive control solution of (I) obtained from a normal mammal and a mammal afflicted with Alzheimer's disease respectively;
(iv) an antibody directed against (I); and
(v) instructional material.
ACTIVITY - Nootropic; neuroprotective.
MECHANISM OF ACTION - None given.
USE - The method is useful for diagnosing oxidant stress syndrome or disease in a mammal involving measuring level of lipid peroxidation, and for identifying a compound and its effective dose, useful for treating Alzheimer's disease (claimed). The oxidative stress syndrome or disease is a neurodegenerative syndrome or disease such as, for example, Alzheimer's disease, Amyotropic Lateral Sclerosis, Down's syndrome, and Parkinson's disease (preferably Alzheimer's disease).
ADVANTAGE - The **isoprostanes** used as molecular markers of lipid peroxidation are chemically stable end products of lipid peroxidation, that are released by phospholipases circulated in the plasma and are excreted in the urine, when compared to the conventional indices of lipid peroxidation which rapidly decompose.
Dwg.0/7
FS CPI EPI
FA AB; DCN
MC CPI: B04-G02; B04-H03C; B11-C07A; B11-C08A; B11-C08D2; B12-K04A5; B12-K04E; D05-H09
EPI: S03-E14H4
TECH UPTX: 20000725
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Measuring the level of (I) comprises obtaining (Ia) from the tissue or body fluid of the mammal and isolating (I) by using a total lipid solvent extraction method, followed by assaying and quantifying the level of (I). The assay is especially a gas chromatography/mass spectrometry assay comprising a synthetic homologous **isoprostane** standard, when quantifying is performed using peak area or peak height ratios. The elevated level of lipid peroxidation comprises an elevated level of reactive oxygen species (ROS), and an elevated level of inflammation which comprises an elevated cyclooxygenase (COX) activity. (I) is iPF2alpha-III, iPF2alpha-VI or 8,12-iso-iPF2alpha-VI. (Ia) or (Ib) is obtained from the tissue or body fluid of the mammal. The tissue is brain frontal or temporal pole tissue and the body fluid is cerebrospinal fluid (CSF), plasma or urine. (II) is an antioxidant or antiinflammatory compound which is administered at a series of concentrations effective to inhibit the activity of COX enzyme or reduce the level of ROS in the brain tissue.

=> d all abeq tech tot

L93 ANSWER 1 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1999-253847 [21] WPIX
DNC C1999-074141
TI Use of **isoprostane** measurements for assessing oxidative stress in an organism.
DC B04 D16
IN CALLEWAERT, D M; KIM, H; MORROW, J D; ROBERTS, L J
PA (OXFO-N) OXFORD BIOMEDICAL RES INC; (UYVA-N) UNIV VANDERBILT
CYC 1
PI US 5891622 A 19990406 (199921)* 16p C12Q001-00 <--
ADT US 5891622 A Provisional US 1997-38496P 19970225, US 1998-28543 19980224
PRAI US 1997-38496P 19970225; US 1998-28543 19980224
IC ICM **C12Q001-00**
ICS **C12Q001-02; C12Q001-26**
AB US 5891622 A UPAB: 20011211
NOVELTY - Method for assessing oxidative stress in an organism comprising measuring the amount of free, esterified and glucuronidated forms of

isoprostanes (IPs), is new.

DETAILED DESCRIPTION - The method of assessing oxidative stress in vivo comprises measuring the amount of free, esterified and glucuronidated forms of IPs, and comparing the measured amount with a healthy control sample where a relatively increased amount of IPs in the test sample indicates oxidative stress.

An INDEPENDENT CLAIM is also included for a method to assess oxidative stress in vivo by measuring the amount of glucuronidated IPs and comparing the measured amount with a control sample where a relatively increased amount of glucuronidated IPs in the test sample indicates oxidative stress.

USE - The methods can be used for the assessment of oxidative stress and disorders such as hepatorenal syndrome, atherosclerosis and carcinogenesis.

The levels of 8EPGF2 in urine specimens obtained from heavy smokers were measured by ELISA without pretreatment or GC/NICI-MS after purification of urine samples by a 2 column method. The 8EPGF2 levels in smokers urine specimens were 1.5 to 3-fold higher than those of non-smokers as obtained by both ELISA and GC/NICI-MS. The levels of 8EPGF2 measured by ELISA in urine specimens were 4 to 15-fold higher than the levels of these measured by GC/NICI-MS.

DESCRIPTION OF DRAWING(S) - The graph shows retention of 8-epi-prostaglandin F2 alpha (8EPGF2) in an immunoaffinity column.

Dwg.0/7

FS CPI
FA AB; DCN
MC CPI: B04-B04B1; B04-B04D4; B04-B04H; B04-B04L; B04-H03; B04-H03C; B04-L01; B10-C04A; B11-C07A; B11-C08E3; B12-K04A; D05-H09
TECH UPTX: 19990603

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Sample: The biological sample may be plasma, cerebrospinal fluid, bile, joint fluid and especially urine. The measuring step is preferably an immunoassay carried out after hydrolyzation of the sample.

Preferred **Isoprostanes**: The IPs measured is 8-epi-prostaglandin F2alpha (8EPGF2).

L93 ANSWER 2 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 1994-083360 [10] WPIX
DNN N1994-065081 DNC C1994-038242
TI New **isoprostane**-protein conjugates - used for the prodn. of antibodies and for the measurement of **isoprostanes** in biological samples.
DC B03 B04 B05 D16 S03
IN KAN, W; MAXEY, K M
PA (CAYM-N) CAYMAN CHEM CO
CYC 18
PI WO 9404921 A1 19940303 (199410)* EN 19p G01N033-53 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU JP
AU 9350099 A 19940315 (199428) G01N033-53 <--
ADT WO 9404921 A1 WO 1993-US7630 19930811; AU 9350099 A AU 1993-50099 19930811
FDT AU 9350099 A Based on WO 9404921
PRAI US 1992-928484 19920811
REP 02Jnl.Ref; EP 166583
IC ICM **G01N033-53**
ICS C07K017-00; C08H001-00
AB WO 9404921 A UPAB: 19940421

An **isoprostane**-protein conjugate comprising an **isoprostane** covalently bonded to a protein is claimed.

Pref. the **isoprostane** is of formula (I)-(IV). The protein may be e.g. acetylcholinesterase, horseradish peroxidase, alkaline phosphatase, beta-galactosidase, glucose oxidase, urease, glucose-6-dehydrogenase, penicillinase, serum albumins, thyroglobulins or keyhole limpet haemocyanin.

USE - The measurement of **isoprostanes** can be used in the diagnosis of oxidative stress and oxidative tissue damage, including

ischemic tissue re-perfusion injury, oxidant stress from environmental sources such as ozone pollution and oxidative lung injury in the respiratory distress syndromes of prematurity and adult acute pulmonary trauma. It can also be used in prognosis in e.g. victims of myocardial infarction, stroke, closed head injury, asphyxiation or cold water immersion. The conjugates can also be used for the prodn. of antibodies and in studies of **isoprostane** binding proteins and receptors.
Dwg.0/0
FS CPI EPI
FA AB; GI; DCN
MC CPI: B04-G01; B04-H03; B04-L03A; B04-L05A; B04-N01; B04-N04; B11-C07A; B12-K04; D05-A01A4; D05-A01B; D05-H09; D05-H11
EPI: S03-E14H4

=> fil hcaplus
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FILE COVERS 1907 - 29 Jan 2002 VOL 136 ISS 5
FILE LAST UPDATED: 28 Jan 2002 (20020128/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1907 to the present. Bibliographic information and abstracts were added in 2001 for over 3.8 million records from 1907-1966.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

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L136 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:185403 HCAPLUS
DN 131:41645
TI Simultaneous HPLC analysis of arachidonic acid metabolites in biological samples with simple solid phase extraction
AU Kim, Hyung-Gun; Huh, Young-Na; Park, Kun-Suk
CS Department of Pharmacology, College of Medicine, Dankook University, Cheonan, 330-714, S. Korea
SO Korean J. Physiol. Pharmacol. (**1998**), 2(6), 779-786

CODEN: KJPPFS; ISSN: 1226-4512
PB Korean Physiological Society
DT Journal
LA English
AB A reversed-phase high-performance liq. chromatog. (RP-HPLC) has been developed to analyze the metabolites of arachidonic acid based on the specificities of UV absorption of these various metabolites and is sensitive to the nanogram level. This procedure makes it possible to ext. complex mixts. of eicosanoids efficiently with a single step and to analyze them simultaneously by RP-HPLC from biol. samples using octadesylsilyl silica extn. column and PGB2 as an internal std. The **cyclooxygenase** products {prostaglandin (PG)D2, PGE1, PGE2, PGF1.alpha., PGF2.alpha., 6-keto-PGF1.alpha., and thromboxane B2 (TXB2)} and lipid peroxidn. product, **isoprostanes**, of arachidonic acid were monitored by one isocratic HPLC system at 195 nm wavelength. The lipoxygenase products {leukotriene(LT)B4, LTC4, LTD4, and 5-hydroxyeicosatetraenoic acid (5-HETE), 12-HETE, 15-HETE} were measured by another isocratic HPLC system at 280 nm for LTs and 235 nm for HETEs. This method provides a simple and reliable way to ext. and assess quant. the final arachidonic acid metabolites.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:81638 HCAPLUS
DN 130:136305
TI Lipid hydroperoxides to detect brain injury
IN Beal, M. Flint; Koroshetz, Walter J.
PA The General Hospital Corporation, USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9904268	A1	19990128	WO 1998-US14829	19980715 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9884106	A1	19990210	AU 1998-84106	19980715 <--
PRAI US 1997-52948		19970717 <--		
US 1997-55143		19970812 <--		
WO 1998-US14829		19980715 <--		

AB Disclosed are methods for diagnosing brain injury by detecting an elevated level of lipid hydroperoxide or a degradative product thereof in a body fluid, such as plasma. Elevated lipid hydroperoxide levels also are correlated with the extent and severity of brain injury, as well as patient prognosis and conventional scales for assessing brain injury. Also disclosed are methods for detg. the likelihood that a patient will develop, or has developed, vasospasm. Such methods entail detecting a decrease in ascorbic acid levels in a body fluid of a patient.
IT **27415-26-5**, 8-epi-Pgf2.alpha.
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(lipid hydroperoxides to detect brain injury)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:45058 HCAPLUS

DN 130:121861
TI Method and compositions to assess oxidative stress in vivo by determining prostaglandin F2-like compounds and their metabolites
IN Roberts, L. Jackson, II; Morrow, Jason D.
PA Vanderbilt University, USA
SO U.S., 15 pp., Cont.-in-part of U.S. 5,700,654.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5858696	A	19990112	US 1997-912440	19970818 <--
	US 5700654	A	19971223	US 1994-304147	19940912 <--
PRAI	US 1991-715419		19910614 <--		
	US 1994-304147		19940912 <--		

AB This invention relates to a method to assess oxidative stress in vivo by quantification of prostaglandin F2-like compds. and their metabolites produced by a noncyclooxygenase free radical-catalyzed mechanism. The major urinary metabolite of 8-iso-prostaglandin F2.alpha. was analyzed by GC-neg. ion chem. ionization-mass spectrometry and by electron ionization-MS.
IT **27415-26-5**, 8-Iso-PGF2.alpha.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic study of; method and compns. to assess oxidative stress in vivo by detg. prostaglandin F2-like compds. and their metabolites)
IT **39391-18-9, Cyclooxygenase**
RL: MSC (Miscellaneous)
(prostanoids not derived from, detn. of; method and compns. to assess oxidative stress in vivo by detg. prostaglandin F2-like compds. and their metabolites)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:706994 HCAPLUS
DN 130:105032
TI Improved blood substitute evaluation of its effects on human endothelial cells
AU Simoni, Jan; Simoni, Grace; Martinez-Zagyilan, Raul; Wesson, Donald E.; Lox, Charles D.; Prien, Samuel D.; Kumar, Ramana Vijay
CS Departments of Surgery, Texas Tech University Health Sciences Center, Lubbock, TX, 79430, USA
SO ASAIO J. (**1998**), 44(5), M356-M367
CODEN: AJOUET; ISSN: 1058-2916
PB Lippincott-Raven Publishers
DT Journal
LA English
AB The authors have previously documented that appropriate chem. and pharmacol. modification of the Hb mol. are required to attenuate certain pathophysiol. reactions of the reticuloendothelium. The current study further investigates the mol. responses of human coronary artery endothelial cells to a high concn. (0.4 mmol) of 1) unmodified bovine Hb; and 2) an improved **blood** substitute that comprises Hb cross-linked intramolecularly with o-ATP and intermolecularly with o-adenosine, and conjugated with reduced glutathione. In this study, the scavenging effect of Hbs toward nitric oxide (NO) was evaluated by the measurement of nitrite (NO2-) and nitrate (NO3-) formation. The pro-oxidant effect of Hb on endothelial cells was examd. by the measurement of intracellular reduced glutathione, and by monitoring the formation of **lipid** hydroperoxides and 8-iso prostaglandin F2.alpha., a novel potent vasoconstrictor, which is produced by a noncyclooxygenase mechanism involving free radical catalyzed **peroxidn**. of arachidonic acid. The inflammatory reactions of endothelial cells were evaluated by the expression of the adhesion mol., intracellular adhesion mol.-1, and the activation of nuclear transcription

factor, nuclear factor .kappa.B. In addnl., endothelial cell responses were investigated by **anal.** of intracellular ionized calcium concns. Results indicate that unmodified Hb in a concn. of 0.4 mmol/L can aggravate endothelial cell oxidative and inflammatory responses. This Hb produced a significant ($p < 0.01$) depletion of reduced glutathione, acceleration of **lipid peroxidn.**, and a greater influx of Ca2+. The formation of 8-iso prostaglandin F2.alpha. increased compared with the control cells ($p < 0.01$). Unmodified Hb was found to be a potent scavenger of NO, great activator of nuclear factor .kappa.B, and a stimulator of intracellular adhesion mol.-1 expression. Contrarily, the improved **blood** substitute did not appear to induce oxidative stress nor to increase the intracellular Ca2+. The concn. of 8-iso prostaglandin F2.alpha. was similar to that in the control cells, whereas the formation of NO2-/NO3- was much lower ($p < 0.05$) than in the unmodified Hb group. The effect of an improved **blood** substitute can be linked with the anti-inflammatory and cytoprotective properties of adenosine, which is used as a cross-linker and surface modifier, and the type of the chem. modification procedure that lowers Hb pro-oxidant potential.

IT **27415-26-5**, 8-Iso prostaglandin F2.alpha.
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(effect of blood substitute on human endothelial cell 8-iso prostaglandin F2.alpha.)

RE.CNT 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:400525 HCAPLUS
DN 129:117928
TI Radioimmunoassay of 8-iso-prostaglandin F2.alpha.: an index for oxidative injury via free radical catalyzed **lipid peroxidation**
AU Basu, S.
CS Department of Geriatrics, Faculty of Medicine, Uppsala University, Uppsala, S-751 25, Swed.
SO Prostaglandins, Leukotrienes Essent. Fatty Acids (**1998**), 58(4), 319-325
CODEN: PLEAEU; ISSN: 0952-3278
PB Churchill Livingstone
DT Journal
LA English
AB 8-Iso-prostaglandin F2.alpha. (8-iso-PGF2.alpha.), a major F2-**isoprostane**, is biosynthesized in vivo through non-enzymic free radical-catalyzed **peroxidn.** of arachidonic acid. The levels of F2-**isoprostanes** both free in the circulation and esterified to the tissue phospholipids increase intensely in animal models of oxidant injury. This study presents the development and validation of a RIA of 8-iso-PGF2.alpha. for the measurement of this substance in the body fluids. Furthermore, its application in normal human volunteers, a pharmacokinetic study performed in rabbits with 8-iso-PGF2.alpha. and hepatic **lipid peroxidn.** in rats is reported. An antibody was raised in rabbits by immunization with 8-iso-PGF2.alpha. coupled to BSA at the carboxylic acid by 1,1'-carbonyldiimmidazole method. The cross-reactivity of the antibody with 8-iso-15-keto-13, 14-dihydro-PGF2.alpha., 8-iso-PGF2.beta., PGF2.alpha., 15-keto-PGF2.alpha., 15-keto-13, 14-dihydro-PGF2.alpha., TXB2, 11.beta.-PGF2.alpha., 9.beta.-PGF2.alpha. and 8-iso-PGF3.alpha. was 1.7, 9.8, 1.1, 0.01, 0.01, 0.1, 0.03, 1.8 and 0.6%, resp. The intraassay precision was 14.5% (CV) at the level of 64 pg/0.1 mL and 12.2% with 512 pg/0.1 mL in the human plasma. Similarly, intra-assay accuracy was 95.6% and 101% for the low and the high std., resp. The detection limit was about 23 pmol/l. The appearance and disappearance of 8-iso-PGF2.alpha. in the blood and urine following i.v. administration of 8-iso-PGF2.alpha. in the rabbit was rapid. Free 8-iso-PGF2.alpha. levels in plasma and urine from normal human volunteers are evaluated and found to correlate with the obtained values by gas chromatog.-mass spectrometry methods from other studies. The levels of free 8-iso-PGF2.alpha. in the plasma and urine

increased 7- and 102-fold, resp., after CCl4 administration to rats. Thus, this 8-iso PGF2.alpha. RIA method is relevant to apply in the oxidative injury studies as an index of in vivo **lipid peroxidn.** through free radical catalysis mechanism.

IT **27415-26-5**, 8-Iso-prostaglandin F2.alpha.
RL: ANT (Analyte); ANST (Analytical study)
(RIA of 8-iso-prostaglandin F2.alpha. as an index for oxidative injury via free radical catalyzed **lipid peroxidn.**)

L136 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:12187 HCAPLUS
DN 128:110905
TI Improved quantification of 8-epi-prostaglandin F2.alpha. and F2-**isoprostanes** by gas chromatography/triple-stage quadrupole mass spectrometry: partial **cyclooxygenase**-dependent formation of 8-epi-prostaglandin F2.alpha. in humans
AU Schweer, Horst; Watze, Bernhard; Seyberth, Hannsjorg W.; Nusing, Rolf M.
CS Children's Hospital, Philipps University Marburg, Marburg, D-35033, Germany
SO J. Mass Spectrom. (**1997**), 32(12), 1362-1370
CODEN: JMSPFJ; ISSN: 1076-5174
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB F2-**isoprostanes** are considered to be novel markers of lipid peroxidn. To study the in vivo formation of F2-**isoprostanes**, an improved method was developed for isotope diln. assays involving gas chromatog./triple-stage quadrupole mass spectrometry (GC/MS/MS) including thin-layer chromatog. (TLC) (sum of all F2-**isoprostanes**) and high-performance liq. chromatog. (HPLC) purifn. (prostaglandin F2.alpha. (PGF2.alpha.) and 8-epi-PGF2.alpha.). Following the addn. of isotopically labeled prostaglandins to urine, the sample was acidified and applied to a C18 cartridge. After elution, prostaglandins were derivatized to pentafluorobenzyl esters and subjected to TLC. A broad zone was scratched off, **isoprostanes** were eluted and after formation of their trimethylsilyl ether derivs. the sum of F2-**isoprostanes** was detd. by GC/MS/MS. For the detn. of PGF2.alpha. and 8-epi-PGF2.alpha. prior to trimethylsilylation an addnl. HPLC step was performed and the fractions contg. PGF2.alpha. and 8-epi-PGF2.alpha. were analyzed by GC/MS/MS. Using this technique, 8-epi-PGF2.alpha. concns. in urine samples as low as 5 pg ml-1 could be detd. with high accuracy. The excretion rates of **isoprostanes** were studied in comparison with the classical prostaglandins in three different groups: healthy adults, healthy children and children with hyper-PGE syndrome (HPS), a pathol. situation assocd. with a stimulated PGE2 synthesis. F2-**isoprostanes** represented the main arachidonic acid metabolites in these groups and 8-epi-PGF2.alpha. excretion was comparable in its amt. to the classical prostanoids. To delineate the **cyclooxygenase**-catalyzed contribution, the influence of indomethacin, an inhibitor of **cyclooxygenases**, on F2-**isoprostane** formation in healthy adults and in HPS children was analyzed. Significantly decreased excretion rates were obsd. 2 days after indomethacin administration for all prostanoids, including F2-**isoprostanes** and 8-epi-PGF2.alpha.. However, the suppression of F2-**isoprostanes** and 8-epi-PGF2.alpha. excretion rates was less pronounced in comparison with the classical prostanoids. An improved and reliable method for the detn. of F2-**isoprostanes** and esp. 8-epi-PGF2.alpha., has been developed. The data obtained on human urine samples indicates a contribution of the **cyclooxygenase** pathway to the formation of **isoprostanes**.

IT **27415-26-5**, 8-epi-Prostaglandin F2.alpha.
RL: ANT (Analyte); BPR (Biological process); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(improved quantification of 8-epi-PGF2.alpha. and F2-**isoprostanes** by gas chromatog./triple-stage quadrupole mass

spectrometry and partial **cyclooxygenase**-dependent formation of 8-epi-PGF2.alpha. in humans)

IT **39391-18-9, Cyclooxygenase**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(improved quantification of 8-epi-PGF2.alpha. and F2-**isoprostanes** by gas chromatog./triple-stage quadrupole mass spectrometry and partial **cyclooxygenase**-dependent formation of 8-epi-PGF2.alpha. in humans)

L136 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:576125 HCAPLUS
DN 127:273177
TI Reduction of urinary 8-epi-prostaglandin F2.alpha. during cyclooxygenase inhibition in rats but not in man
AU Bachi, Angela; Brambilla, Raffaella; Fanelli, Roberto; Bianchi, Roberto; Zuccato, Ettore; Chiabrando, Chiara
CS Inst. Ric. Farmacol. "Mario Negri", Milan, 20157, Italy
SO Br. J. Pharmacol. (**1997**), 121(8), 1770-1774
CODEN: BJPCBM; ISSN: 0007-1188
PB Stockton
DT Journal
LA English
AB 8-Epi-prostaglandin (PG) F2.alpha., a major F2 **isoprostane**, is produced in vivo by free radical-dependent **peroxidn.** of **lipid**-esterified arachidonic acid. Both cyclo-oxygenase isoforms (COX-1 and COX2) may also form free 8-epi-PGF2.alpha. as a minor product. It has been recently seen in human volunteers that the overall basal formation of 8-epi-PGF2.alpha. in vivo is mostly COX-independent and urinary 8-epi-PGF2.alpha. is therefore an accurate marker of 'basal' oxidative stress in vivo. To test the validity of this marker in the rat, the authors evaluated in vivo the effect of COX inhibition on the formation of 8-epi-PGF2.alpha. vs. prostanoids. Two structurally unrelated COX inhibitors (naproxen: 30 mg/kg/day; indomethacin: 4 mg/kg/day) were given i.p to rats kept in metabolic cages. In vivo formation of 8-epi-PGF was assessed by measuring its urinary excretion. Prostanoid biosynthesis was assessed by measuring urinary excretion of major metabolites of thromboxane (TX) and prostacyclin (2,3-dinor-TXB1 and 2,3-dinor-6-keto-PGF2.alpha.). All compds. were selectively measured by immunopurifn./gas chromatog.-mass spectrometry. Naproxen reduced urinary excretion of 2,3-dinor-TXB1 and 2,3-dinor-6-keto-PGF1.alpha. but, unexpectedly, also that of 8-epi-PGF2.alpha. (82, 49, and 52% inhibition, resp.). Indomethacin had a similar effect (77, 69 and 55% inhibition). Esterified 8-epi-PGF2.alpha. in liver and plasma remained unchanged after indomethacin. These findings prompted the authors to re-assess the contribution of COX activity to the systemic prodn. of 8-epi-PGF2.alpha. in man. The authors gave naproxen (1 g day-1) to healthy subjects (four nonsmokers and four smokers). Urinary 8-epi-PGF2.alpha. remained unchanged in the two groups (9,63 before vs. 10.24 after and 20.14 vs. 19.03 ng h-1 1.73 m-2), whereas there was a marked redn. of major urinary metabolites of thromboxane and prostacyclin (about 90% for both 11-dehydro-TXB2 and 2,3-dinor-TXB2; >50% for 2,3-dinor-6-keto-PGF1.alpha.). the authors conclude that a significant amt. of COX-dependent 8-epi-PGF2.alpha. is present in rat but not in human urine under normal conditions. To investigate whether rat COX-1 produces 8-epi-PGF more efficiently than human COX-1, the authors measured the ex vivo formation of 8-epi-PGF and TXB simultaneously in whole clotting blood. Serum levels of 8-epi-PGF and TXB were similar in rats and man. This implies that urinary 8-epi-PGF cannot be used as an index of near-basal oxidant stress in rats. On the other hand, the authors' data further confirm the validity of this marker in man.

IT **27415-26-5**, 8-epi-Prostaglandin F2.alpha.
RL: BOC (Biological occurrence); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(redn. of urinary 8-epi-prostaglandin F2.alpha. during cyclooxygenase inhibition in rats but not in man)

L136 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:560155 HCAPLUS
DN 127:232856
TI Platelet activation and **lipid peroxidation** in patients with acute ischemic stroke
AU Van Kooten, Fop; Ciabattoni, Giovanni; Patrono, Carlo; Dippel, Diederik W. J.; Koudstaal, Peter J.
CS Department of Neurology, University Hospital Rotterdam, Rotterdam, 3015 GD, Neth.
SO Stroke (Dallas) (**1997**), 28(8), 1557-1563
CODEN: SJCCA7; ISSN: 0039-2499
PB American Heart Association
DT Journal
LA English
AB Both platelet activation and **lipid peroxidn.** are potential sources of vasoactive eicosanoids that can be produced via the cyclooxygenase pathway, ie, thromboxane (TX) A2, or by free radical-catalyzed **peroxidn.** of arachidonic acid, i.e., **isoprostanes.** The biosynthesis of TXA2 and F2-**isoprostanes,** as reflected by the urinary excretion of 11-dehydro-TXB2 and 8-epi-prostaglandin (PG) F2a, resp., was investigated in 62 consecutive patients (30 men, 32 women; mean 67 .+-. 14 yr) with acute ischemic stroke. At least 2 consecutive 6-h **urine** samples were obtained during the first 72 h after onset of symptoms. Urinary eicosanoids were measured by previously described RIAs. Repeated periods of enhanced thromboxane biosynthesis were found in 52% of patients. Urinary 11-dehydro-TXB2 averaged 221 .+-. 207 pmol/mmol creatinine in 30 patients treated with cyclooxygenase inhibitors (mostly aspirin) at the time of study vs. 392 .+-. 392 in 32 untreated patients. The corresponding values for 8-epi-PGF2.alpha. excretion were 74 .+-. 42 and 83 .+-. 65 pmol/mmol creatinine. The correlation between the 2 metabolites was moderate in both untreated patients and patients with cyclooxygenase inhibitors. In a multiple regression **anal.,** increased thromboxane prodn. was independently assocd. with severity of stroke on admission, atrial fibrillation, and treatment with cyclooxygenase-inhibiting drugs. Thus, during the first few days after an acute ischemic stroke (1) platelet activation occurs repeatedly in a cyclooxygenase-dependent fashion; (2) platelet activation is not assocd. with concurrent changes in **isoprostane** biosynthesis; (3) platelet activation is independently assocd. with stroke severity and atrial fibrillation; and (4) **isoprostane** biosynthesis is largely independent of platelet cyclooxygenase activity.
IT **27415-26-5,** 8-epi-Prostaglandin F2.alpha.
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(platelet activation and **lipid peroxidn.** in men and women with acute ischemic stroke)

L136 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:469520 HCAPLUS
DN 127:156822
TI Isolation and measurement of urinary 8-iso-prostaglandin F2.alpha. by high-performance liquid chromatography and gas chromatography-mass spectrometry
AU Ferretti, Aldo; Flanagan, Vincent P.
CS Nutrient Requirements and Functions Laboratory, Beltsville Human Nutrition Research Center, US Department of Agriculture, ARS, Beltsville, MD, 20705, USA
SO J. Chromatogr., B: Biomed. Sci. Appl. (**1997**), 694(2), 271-276
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier
DT Journal
LA English
AB 8-Iso-Prostaglandin F2.alpha. (8-iso-PGF2.alpha.) is a product of free radical-catalyzed peroxidn. of arachidonic acid. Measurement of its

urinary excretion has been proposed as an index of oxidative status in vivo. A stable isotope diln. for its quantification by gas chromatog.-electron capture chem. ionization mass spectrometry is described. Sample cleanup required the combined use of HPLC and thin-layer chromatog. The inter-assay R.S.D. in two sep. detns. was 1.6 and 2.3%. The accuracy of the assay was evaluated through recovery expts. The equation of the regression plot correlating the amts. added and recovered was y = 0.91x-0.31, r = 0.9916. The pair of fragment ions ([M-181]-) at m/z 569 and m/z 573 was monitored for quantification. The mean 8-iso-PGF2.alpha. excretion rate was 528 (S.D.) ng per day in five male volunteers and 730 ng per day in six females. Intake of 80 mg of lycopene per day by eleven volunteers for four weeks resulted in a non-significant redn. of 8-iso-PGF2.alpha. excretion.

IT **27415-26-5**, 8-Iso-prostaglandin F2.alpha.
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(isolation and measurement of urinary 8-iso-prostaglandin F2.alpha. by high-performance liq. chromatog. and gas chromatog.-mass spectrometry)

L136 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:404894 HCAPLUS
DN 127:131096
TI Enzymic synthesis of dioxygen-18-labeled 8-epi-prostaglandin F2.alpha. and its use in quantitative GC-tandem MS
AU Tsikas, Dimitrios; Schwedhelm, Edzard; Gutzki, Frank-Mathias; Jahn, Olaf; Fakistas, Panagiotis; Frolich, Jurgen C.
CS Institute of Clinical Pharmacology, Hannover Medical School, Hannover, D-30625, Germany
SO J. Labelled Compd. Radiopharm. (**1997**), 39(6), 531-540
CODEN: JLCRD4; ISSN: 0362-4803
PB Wiley
DT Journal
LA English
AB 8-Epi-Prostaglandin F2.alpha. (8-epi-PGF2.alpha.) is an endogenous potent vasoconstrictor, non-**cyclooxygenase**-derived prostanoid which may be suitable as an index of oxidative stress in living organisms. For quant. detn. of 8-epi-PGF2.alpha. in biol. fluids we describe here the one-step enzymic synthesis of [1,1-18O2]-8-epi-PGF2.alpha. starting from com. available unlabeled 8-epi-PGF2.alpha., H218O, and an unspecific porcine liver esterase. The isolated and purified reaction product was found to contain 80.3% [1,1-18O2]-8-epi-PGF2.alpha., 17.7% [1,1-18O16O]-8-epi-PGF2.alpha., and only 2.0% unlabeled 8-epi-PGF2.alpha.. [1,1-18O2]-8-epi-PGF2.alpha. is demonstrated to be a suited internal std. for quant. detn. of 8-epi-PGF2.alpha. in human urine by GC-MS/MS. In 5 mL aliquots of human urine samples from spontaneous micturation on different days, 8-epi-PGF2.alpha. was found to be present at concns. of 300 and 490 pg/mg creatinine, resp.

IT **27415-26-5**, 8-epi-Prostaglandin F2.alpha.
RL: ANT (Analyte); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(dioxygen-18-labeled 8-epi-prostaglandin F2.alpha. enzymic prepn. and use in quant. GC-tandem MS)

L136 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:283784 HCAPLUS
DN 126:312364
TI Simultaneous Solid Phase Extraction, Derivatization, and Gas Chromatographic Mass Spectrometric Quantification of Thromboxane and Prostacyclin Metabolites, Prostaglandins, and **Isoprostanes** in Urine
AU Wuebert, Joachim; Reder, Elke; Kaser, Andrea; Weber, Peter C.; Lorenz, Reinhard L.
CS Institute for Prophylaxis and Epidemiology of Cardiovascular Disease, University of Munich, Munich, 80336, Germany
SO Anal. Chem. (**1997**), 69(11), 2143-2146
CODEN: ANCHAM; ISSN: 0003-2700

PB American Chemical Society
DT Journal
LA English
AB The current **anal.** methods for the various prostanoids require a sep. and extended sample workup, derivatization, and gas chromatog./mass spectrometric detection of each compd. Therefore, the authors developed and validated a rapid method for the common purifn., derivatization, and GC/MS detn. of 11-dehydrothromboxane B2, 2,3-dinor-6-keto-PGF1a, PGF2a, PGE2, PGD2, and **isoprostanes** in **urine**. A single reversed-phase solid-phase extn. step and modified reaction conditions yielded excellent sample purifn. at high recoveries and efficient derivatization for all compds. in one vial. The method allows the simultaneous quantification of these index metabolites of systemic thromboxane and prostacyclin synthesis, renal prostaglandin formation, and nonenzymic in vivo **lipid peroxidn.** in a single GC/MS run with high sensitivity and precision.
IT **27415-26-5**, 8-epi-PGF2.alpha.
RL: ANT (Analyte); ANST (Analytical study)
(simultaneous solid phase extn., derivatization, and GC-MS quantification of thromboxane and prostacyclin metabolites, prostaglandins, and **isoprostanes** in urine)

L136 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:5410 HCAPLUS
DN 126:44581
TI Enzyme immunoassay for 8-epi-prostaglandin F2.alpha. and its preliminary clinical application
AU Wang, Zhaoyue; Wang, Shanxi; Ruan, Changgeng
CS Thrombosis and Hemostasis Research Unit, Suzhou Medical College, Suzhou, 215007, Peop. Rep. China
SO Zhonghua Yixue Jianyan Zazhi (**1996**), 19(4), 238-241
CODEN: CHCCDO; ISSN: 0253-973X
PB Zhonghua Yixuehui
DT Journal
LA Chinese
AB The plasma 8-epi-prostaglandin F2.alpha. (8-epi-PGF2.alpha.) levels in 17 normal patients, 18 patients with acute cerebral thrombosis, and 16 patients with chronic renal failure were assayed by an acetylcholine esterase-labeled enzyme immunoassay (EIA) after the binding parameters of EIA were obtained. For the EIA, 8-epi-PGF2.alpha. was linked to the amino groups of lysines of acetylcholenesterase to prep. the enzyme tracer. To produce antibodies for the EIA, 8-epi-PGF2.alpha. was conjugated to HSA, and the conjugate was s.c. injected into rabbits. The best antiserum used for the EIA was obtained after the 5th booster, presenting a high titer (1/300000). Its linear range was 2-125 pg ml-1 with an IC50 of 8 ng L-1. The cross reactivities with other PGs and related metabolites were negligible, and the intra- and inter-assay variabilities were 4.8% (n=14) and 7.5% (n=9), resp. The plasma 8-epi-PGF2.alpha. in patients with acute cerebral thrombosis was significantly higher than the normal level, and hemodialysis decreased the concns. of the 8-epi-PGF2.alpha. in CRF patients to normal levels. In conclusion, the EIA for 8-epi-PGF2.alpha. showed a high sensitivity and specificity, and the clin. results suggest that 8-epi-PGF2.alpha. can be used as a index of **lipid peroxidn.** and related diseases.
IT **27415-26-5**, 8-Epi-Prostaglandin F2.alpha.
RL: ANT (Analyte); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(enzyme immunoassay for 8-epi-prostaglandin F2.alpha. and its preliminary clin. application in humans with acute cerebral thrombosis or chronic renal failure)

L136 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:189330 HCAPLUS
DN 124:220702
TI Measurement of urinary 8-epi-prostaglandin F2.alpha., a novel index of **lipid peroxidation** in vivo, by immunoaffinity

extraction/gas chromatography-mass spectrometry. Basal levels in smokers and nonsmokers
AU Bachi, Angela; Zuccato, Ettore; Baraldi, Monica; Fanelli, Roberto; Chiabrando, Chiara
CS Ist. Ricerche Farmacol. 'Mario Negri', Milan, Italy
SO Free Radical Biol. Med. (**1996**), 20(4), 619-24
CODEN: FRBMEH; ISSN: 0891-5849
DT Journal
LA English
AB 8-Epi-prostaglandin F2.alpha.-prostaglandin F2.alpha. (8-epi-PGF2.alpha.) is an F2-**isoprostane** recently identified as a marker of free radical-catalyzed **lipid peroxidn.** in vivo and potential mediator of oxidative damage. Currently, endogenous 8-epi-PGF2.alpha. is measured by gas chromatog.-mass spectrometry after lengthy sample prepn. The authors extd. and purified 8-epi-PGF2.alpha. antiserum, raised in the lab. Quantitation was done by stable-isotope diln. gas chromatog./neg.-ion chem. ionization mass spectrometry, with selected ion recording. Carboxylate anions of the pentafluorobenzyl ester trimethylsilyl ether deriv. of 8-epi-PGF2.alpha. and [2H4]8-epi-PGF2.alpha. were monitored (m/z 569 and 573). Basal urinary excretion of 8-epi-PGF2.alpha. can be accurately and rapidly measured by this method. Under normal conditions rats excreted 2.18 ng/24 h. In healthy nonsmoking young volunteers, urinary excretion of 8-epi-PGF2.alpha., measured three times on alternate days, was fairly const. (CV 2-10%). Nonsmokers excreted significantly less 8-epi-PGF2.alpha. than age-matched smokers (8.08 vs. 18.40 ng/h/1.73 m2), as reported by others using different methods.
IT **27415-26-5**, 8-epi-Prostaglandin F2.alpha.
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(epiPGF2.alpha. detn. in urine by immunoaffinity extn. and chromatog./mass spectrometry in relation to smoking in humans)

L136 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:655704 HCAPLUS
DN 123:78957
TI Analysis of F2-**isoprostanes** as indicators of non-enzymic **lipid peroxidation** in vivo by gas chromatography-mass spectrometry: development of a solid-phase extraction procedure
AU Nourooz-Zadeh, J.; Gopaul, N. K.; Barrow, S.; Mallet, A. I.; Aengard, E. E.
CS Department of Medicine, Division of Clinical Pharmacology and Toxicology, University College London, 5 University Street, London, WC1E 6JJ, UK
SO J. Chromatogr., B: Biomed. Appl. (**1995**), 667(2), 199-208
CODEN: JCBBEP
DT Journal
LA English
AB Recently, it was reported that a series of prostaglandin F2-like compds. (F2-**isoprostanes**) are produced in vivo during peroxidn. of arachidonic acid by a mechanism independent of the **cyclooxygenase** pathway. Of these, 8-epi-PGF2.alpha. is shown to be a potent vasoconstrictor. The authors describe an improved method for analyzing F2-**isoprostanes** in biol. fluids. The method involves solid-phase extn. on an octadecylsilane (C18) and an aminopropyl (NH2) cartridge. After conversion to pentafluorobenzyl ester and trimethylsilyl ether derivs., F2-**isoprostanes** are analyzed by neg.-ion chem. ionization mass spectrometry using tetradeuterated PGF2.alpha. as the internal std. The limit of detection of the assay was 10 pg/mL, with a coeff. of variation ranging from 9.4 to 15.1%. Anal. of plasma samples from healthy volunteers revealed no quantifiable levels of free (unesterified) 8-epi-PGF2.alpha.. However, the plasma samples contained 58 to 166 pg/mL of 8-epi-PGF2.alpha. when analyzed for the total (sum of free and esterified) F2-**isoprostanes**. The main advantages of the method lie in the improved recovery, gas chromatog. sepn. and speed compared to existing techniques.
IT **27415-26-5**, 8-epi-PGF2.alpha.

RL: ANT (Analyte); ANST (Analytical study)
(anal. of F2-**isoprostanes** as indicators of nonenzymic **lipid peroxidn.** in vivo by gas chromatog.-mass spectrometry and solid-phase extn.)

L136 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:625452 HCAPLUS
DN 121:225452
TI Mass spectrometry of prostanoids: F2-**isoprostanes** produced by non-**cyclooxygenase** free radical-catalyzed mechanism
AU Morrow, Jason D.; Roberts, Jackson L. II
CS Dep. Pharmacol. and Med., Vanderbilt Univ. Sch. Med., Nashville, TN, 37232, USA
SO Methods Enzymol. (**1994**), 233(OXYGEN RADICALS IN BIOLOGICAL SYSTEMS, PT. C), 163-74
CODEN: MENZAU; ISSN: 0076-6879
DT Journal
LA English
AB This chapter details procedures employed for the anal. of F2-**isoprostanes** from biol. sources. Specific examples are given demonstrating both the utility and limitations of the assay. Procedures are outlined for the anal. of both free F2-**isoprostanes** and **isoprostanes** esterified to phospholipids.
IT **39391-18-9, Cyclooxygenase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mass spectrometry of F2-**isoprostane** prostanoids produced by non-**cyclooxygenase** free radical-catalyzed mechanism)

L136 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:214486 HCAPLUS
DN 120:214486
TI Free radical-induced generation of **isoprostanes** in vivo. Evidence for the formation of D-ring and E-ring **isoprostanes**
AU Morrow, Jason D.; Minton, Tanya A.; Mukundan, Chetan R.; Campbell, Michelle D.; Zackert, William E.; Daniel, Vincent C.; Badr, Kamal F.; Blair, Ian A.; Roberts, L. Jackson, II
CS Sch. Med., Vanderbilt Univ., Nashville, TN, 37232-6602, USA
SO J. Biol. Chem. (**1994**), 269(6), 4317-26
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The authors recently reported the discovery that a series of novel prostaglandin (PG)F2-like compds. (F2-**isoprostanes**) are produced in vivo independent of the cyclooxygenase as products of free radical-catalyzed **lipid peroxidn.** F2-**isoprostanes** are initially formed in situ from arachidonic acid esterified to phospholipids and then released preformed. The authors have now investigated whether PGD2/E2-like **isoprostanes** are also produced by rearrangement of the PGG2-like intermediates involved in **isoprostane** formation. Using a variety of approaches utilizing mass spectrometry, compelling evidence was obtained for the presence of D2/E2-**isoprostane**-contg. phospholipids in the liver (85 .+-. 33 ng/g of liver) and free D2/E2-**isoprostanes** in the circulation (215 .+-. 90 pg/mL) of rats treated with CCl4 to induce **lipid peroxidn.** In untreated rats, levels of D2/E2-**isoprostanes** esterified in liver phospholipids were much lower (0.90 .+-. 0.10 ng/g), and free compds. could not be detected in the circulation (<5 ng/mL). Interestingly, one of the E2-**isoprostanes** that would be expected to be formed in abundance, 8-epi-PGE2, was found to be a potent renal vasoconstrictor, and these effects could be abrogated by SQ29548, a thromboxane receptor antagonist. Further understanding of the biol. consequences of the formation of these novel compds. and factors that influence their formation may provide valuable insights into the pathophysiol. of oxidant injury.

L136 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:555262 HCAPLUS
DN 119:155262
TI Collision-induced dissociation of F2-**isoprostane**-containing phospholipids
AU Kayganich-Harrison, Kathleen A.; Rose, David M.; Murphy, Robert C.; Morrow, Jason D.; Roberts, L. Jackson, II
CS Dep. Pediatr., Natl. Jew. Cent. Immunol. Respir. Med., Denver, CO, 80206, USA
SO J. Lipid Res. (**1993**), 34(7), 1229-35
CODEN: JLPRAW; ISSN: 0022-2275
DT Journal
LA English
AB Free radical-induced lipid peroxidn. results in the prodn. of metabolites of arachidonic acid isomeric with prostaglandin F2.alpha.. The formation of these compds., termed F2-**isoprostanes**, occurs independent of the enzyme **cyclooxygenase**. The discovery that F2-**isoprostanes** can exert potential biol. activity has suggested that they may mediate, to some extent, the biol. responses to oxidant injury. Collision-induced dissocn. of the [M-CH3]- ions from oxidized phospholipids isolated by extn. and normal phase high performance liq. chromatog. from livers of rats treated with CCl4 to induce lipid peroxidn. revealed several mol. species of phospholipids that had the F2-**isoprostane** esterified to the glycerophosphocholine backbone. Collision-induced dissocn. of the [M-CH2CHN(CH3)3]- ion revealed that the F2- **isoprostanes** were primarily esterified at the sn-2-position of the glycerophospholipid as expected. Furthermore, tandem mass spectrometry of the carboxylate anion from the F2-**isoprostane** (m/z 353) resulted in the unique loss of 44 u characteristic of the 1,2-cyclic diol moiety such as that found in the PGF2-ring. These observations indicate that intact phospholipids contg. fatty acyl groups of the **isoprostane** structure can be readily detected with tandem mass spectrometry even when present as minor components in a biol. ext. Although no specific isomer identification can be made from the complex mixt., these techniques establish the existence of these novel metabolites of arachidonic acid esterified to glycerophospholipids.

L136 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:184212 HCAPLUS
DN 118:184212
TI Identification of non-cyclooxygenase-derived prostanoid (F2-**isoprostane**) metabolites in human urine and plasma
AU Awad, Joseph A.; Morrow, Jason D.; Takahashi, Kihito; Roberts, L. Jackson, II
CS Sch. Med., Vanderbilt Univ., Nashville, TN, 37232-6602, USA
SO J. Biol. Chem. (**1993**), 268(6), 4161-9
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB Recently, it was reported that a series of prostaglandin F2-like compds. (F2-**isoprostanes**) capable of exerting potent biol. activity are produced in vivo by free radical-induced **lipid peroxidn**. Their formation is independent of the cyclooxygenase enzyme and has been shown to increase profoundly in animal models of free radical injury and **lipid peroxidn**. This study reports the identification of F-ring **isoprostane** metabolites in human **urine** and plasma utilizing a gas chromatog./mass spectrometric assay for the major urinary metabolite of prostaglandin D2 (9.alpha.,11.beta.-dihydroxy-15-oxo-2,3,18,19-tetranorprost-5-ene-1,20-dioic acid). Evidence confirming these metabolites as tetranor, dicarboxylic acid compds. contg. one double bond, cis-cyclopentane ring hydroxyls, and one keto group similar in structure to the major urinary metabolite of prostaglandin D2 was obtained by **anal**. of human **urine** by electro ionization mass spectrometry. Levels of these metabolites in normal human **urine** were detd. and found to be unaffected by cyclooxygenase inhibitors. Evidence that these metabolites arise from F2-**isoprostanes** was obtained by demonstrating that

(a) marked increases in plasma levels and urinary excretion of these metabolites, which were unaffected by coadministration of indomethacin, occurred in rats administered CCl4 to induce F2-**isoprostane** formation and (b) marked increases in levels of these metabolites in plasma and **urine** resulted from the i.v. infusion of F2-**isoprostanes** into a rat. Quantification of these **isoprostane** metabolites in **urine** and plasma may provide a reliable index of endogenous **isoprostane** prodn. which could prove to be an important advance in our ability to assess oxidant stress in vivo in humans.

=> fil medline
FILE 'MEDLINE' ENTERED AT 09:58:12 ON 29 JAN 2002

FILE LAST UPDATED: 28 JAN 2002 (20020128/UP). FILE COVERS 1958 TO DATE.

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The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

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=> d all l147

L147 ANSWER 1 OF 1 MEDLINE
AN 1999078771 MEDLINE
DN 99078771 PubMed ID: 9861778
TI Portal levels of the **isoprostane** F2 alpha-III, a marker of **lipid peroxidation**, do not correlate with increased portal pressure in cirrhotic patients.
AU Pratico D; Rossi E; Merli M; Riggio O; FitzGerald G A; Violi F
CS Center for Experimental Therapeutics, University of Pennsylvania, School of Medicine, Philadelphia, USA.
SO JOURNAL OF INVESTIGATIVE MEDICINE, (1998 Dec) 46 (9) 430-4.
Journal code: B9K; 9501229. ISSN: 1081-5589.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 19990128
Last Updated on STN: 19990128
Entered Medline: 19990113
AB BACKGROUND: **Isoprostane** F2 **alpha-III** (**iPF2 alpha-III**), a recently described member of a family of prostaglandin F2 **alpha** isomers and a biologically active end-product of **lipid peroxidation**, has been reported to increase portal pressure in cirrhotic rats. We found that its urinary levels were elevated in cirrhotic patients. METHODS: To investigate whether portal levels of **iPF2 alpha-III** were elevated in cirrhotic patients and whether there was a relationship between these levels and the portal pressure in the same

patients, peripheral and portal plasma from cirrhotic patients (n = 18) undergoing elective transjugular intrahepatic portosystemic shunt and appropriate controls (n = 18) were assayed for **iPF2 alpha-III** levels by using a gas chromatography/mass spectrometry assay. Portal pressure was measured in all cirrhotic patients. RESULTS: Cirrhotic patients had higher peripheral plasma levels of **iPF2 alpha-III** [78 (27-150) pg/mL] than controls [18(10-30)pg/mL] (P < 0.001). Portal **iPF2 alpha -III** levels were higher than plasma peripheral levels [129(50-375) pg/mL; P < 0.0001]. No correlation was found between peripheral and portal levels of **iPF2 alpha-III** (Rho = 0.17, P = 0.5). Portal levels of **iPF2 alpha-III** and portal pressure did not correlate (Rho = 0.17, P = 0.49). CONCLUSIONS: This study shows that peripheral and portal levels of **iPF2 alpha-III**, marker of in vivo **lipid peroxidation**, are elevated in liver cirrhosis. There is no correlation between **iPF2 alpha-III** portal levels and the portal pressure observed in these patients. These findings suggest that this biologically active **isoprostane** does not directly contribute to the portal hypertension observed in hepatic cirrhosis.

CT Check Tags: Comparative Study; Female; Human; Male
Aged
Aged, 80 and over
Biological Markers: BL, blood
***Dinoprost: AA, analogs & derivatives**
Dinoprost: BL, blood
Hypertension, Portal: BL, blood
*Hypertension, Portal: PP, physiopathology
Hypertension, Portal: SU, surgery
***Lipid Peroxidation**
*Liver Cirrhosis: BL, blood
Liver Cirrhosis: PP, physiopathology
Liver Cirrhosis: SU, surgery
Mass Fragmentography
Middle Age
Portal Pressure
Portal Vein
Portasystemic Shunt, Transjugular Intrahepatic

RN 551-11-1 (Dinoprost)
CN 0 (8,12-iso-**isoprostane** F2alpha-III); 0 (Biological Markers)

=> d all tot

L161 ANSWER 1 OF 13 MEDLINE
AN 1999034738 MEDLINE
DN 99034738 PubMed ID: 9817703
TI 8-**Isoprostane** as a biomarker of oxidative stress in interstitial lung diseases.
AU Montuschi P; Ciabattoni G; Paredi P; Pantelidis P; du Bois R M; Kharitonov S A; Barnes P J
CS Imperial College School of Medicine at the National Heart and Lung Institute, Department of Thoracic Medicine, Interstitial Lung Disease Unit, Royal Brompton Hospital, London, United Kingdom.
SO AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, **(1998 Nov)** 158 (5 Pt 1) 1524-7.
Journal code: BZS; 9421642. ISSN: 1073-449X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981218

AB Oxidative stress contributes to the pathophysiology of interstitial lung diseases, such as cryptogenic fibrosing alveolitis (CFA), fibrosing alveolitis associated with systemic sclerosis (FASSc) and sarcoidosis. F2-**isoprostanes** are a series of **prostaglandin** (PG) F2-like compounds produced in vivo independent of **cyclooxygenase**, as products of the radical-catalyzed lipid peroxidation. Measurement of the concentrations of F2-**isoprostanes** has proved to be valuable in assessing oxidative stress in vivo. The aim of this study was to measure 8-epi-PGF2alpha concentrations, one of the most abundant F2-**isoprostane** in humans, in bronchoalveolar lavage (BAL) in normal subjects and to compare them to those observed in patients with CFA (n = 9), FASSc (n = 8) and sarcoidosis (n = 10). 8-epi-PGF2alpha was detectable in BAL fluid in normal subjects (9.6 +/- 0.8 pg/ml) and its concentrations were increased approximately 5-fold in patients with CFA (47.4 +/- 7.0, p < 0.001) and FASSc (43.2 +/- 3.3, p < 0. 001). 8-epi-PGF2alpha was also increased in patients with sarcoidosis, although to a lesser extent (12.0 +/- 0.70 pg/ml, p < 0. 01). No correlation between 8-epi-PGF2alpha and either lung function tests or BAL cell types was observed in any group of patients. Our study shows that the level of oxidative stress is enhanced in patients with interstitial lung diseases as reflected by increased concentrations of 8-epi-PGF2alpha in BAL fluid.

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Biological Markers: AN, analysis
Bronchoalveolar Lavage Fluid: CH, chemistry
Bronchoscopy
***Dinoprost: AA, analogs & derivatives**
Dinoprost: AN, analysis
Free Radicals: AN, analysis
Linear Models
Lipid Peroxidation
*Lung Diseases, Interstitial: ME, metabolism
Middle Age
Nitric Oxide: AN, analysis
***Oxidative Stress**
Pulmonary Fibrosis: ME, metabolism
Sarcoidosis: ME, metabolism
Scleroderma, Systemic: ME, metabolism
Tomography, X-Ray Computed

RN 10102-43-9 (Nitric Oxide); **155976-51-5 (8-isoprostane)**; **551-11-1 (Dinoprost)**

CN 0 (Biological Markers); 0 (Free Radicals)

L161 ANSWER 2 OF 13 MEDLINE
AN 1998188223 MEDLINE
DN 98188223 PubMed ID: 9520386
TI IPF2alpha-I: an index of lipid peroxidation in humans.
AU Pratico D; Barry O P; Lawson J A; Adiyaman M; Hwang S W; Khanapure S P; Iuliano L; Rokach J; FitzGerald G A
CS Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA 19104-6100, USA.
NC DK44730 (NIDDK)
HL54500 (NHLBI)
MO IRR0040 (NCRR)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1998 Mar 31)** 95 (7) 3449-54.
Journal code: PV3; 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980501

AB **Isoprostanes** are **prostaglandin** isomers produced from arachidonic acid by a free radical-catalyzed mechanism. Urinary excretion of 8-iso-**prostaglandin** F2alpha, an isomer of the PGG/H synthase (**cyclooxygenase** or **COX**) enzyme product, **prostaglandin** F2alpha (PGF2alpha), has exhibited promise as an index of oxidant stress in vivo. We have developed a quantitative method to measure **isoprostane** F2alpha-I, (IPF2alpha-I) a class I isomer (8-iso-PGF2alpha is class IV), using gas chromatography/mass spectrometry. IPF2alpha-I is severalfold as abundant in human urine as 8-iso-PGF2alpha, with mean values of 737 +/- 20.6 pg/mg creatinine. Both **isoprostanes** are formed in a free radical-dependent manner in low density lipoprotein oxidized by copper in vitro. However, IPF2alpha-I, unlike 8-iso-PGF2alpha, is not formed in a **COX**-dependent manner by platelets activated by thrombin or collagen in vitro. Similarly, **COX** inhibition in vivo has no effect on IPF2alpha-I. Neither serum IPF2alpha-I, an index of cellular capacity to generate the **isoprostane**, nor urinary excretion of IPF2alpha-I, an index of actual generation in vivo, is depressed by aspirin or indomethacin. In contrast, both serum thromboxane B2 and urinary excretion of its 11-dehydro metabolite are depressed by the **COX** inhibitors. Although serum 8-iso-PGF2alpha formation is substantially depressed by **COX** inhibitors, urinary excretion of the compound is unaffected. Urinary IPF2alpha-I is elevated in cigarette smokers compared with controls (1525 +/- 180 versus 740 +/- 40 pg/mg creatinine; $P < 0.01$) and is highly correlated with urinary 8-iso-PGF2alpha ($r = 0.9$; $P < 0.001$). Urinary IPF2alpha-I is a novel index of lipid peroxidation in vivo, which can be measured with precision and sensitivity. It is an abundant F2-**isoprostane** formed in a free radical- but not **COX** -dependent manner. Although 8-iso-PGF2alpha may be formed as a minor product of **COX**, this pathway contributes trivially, if at all, to levels in urine. Urinary excretion of both **isoprostanes** is elevated in cigarette smokers.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Biological Markers
Dinoprost: CH, chemistry
***Dinoprost: UR, urine**
Isomerism
***Lipid Peroxidation**
Oxidative Stress

RN **551-11-1 (Dinoprost)**

CN 0 (Biological Markers)

L161 ANSWER 3 OF 13 MEDLINE

AN 1998165499 MEDLINE

DN 98165499 PubMed ID: 9506655

TI Eight-epi-PGF2alpha: a possible marker of lipid peroxidation in term infants with severe pulmonary disease.

AU Goil S; Truog W E; Barnes C; Norberg M; Rezaiekhaligh M; Thibeault D

CS The Children's Mercy Hospital, Department of Pediatrics, The University of Missouri-Kansas City School of Medicine, 64108-9898, USA.

SO JOURNAL OF PEDIATRICS, **(1998 Feb)** 132 (2) 349-51.
Journal code: JLZ; 0375410. ISSN: 0022-3476.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199804

ED Entered STN: 19980410
Last Updated on STN: 19980410
Entered Medline: 19980401

AB A **prostaglandin** F2-like compound, 8-epi-PGF2alpha, formed from oxidation of arachidonate, has been proposed as an indicator of lipid peroxidation. We determined whether tracheal aspirate or urinary 8-epi-PGF2alpha levels would differ over time or between infants in a control group and infants with severe respiratory failure. We correlated

tracheal aspirate 8-epi-PGF2alpha levels with the fraction of inspired **oxygen** and with mean airway pressures at 24 and 48 hours of life. Levels in tracheal aspirates were in the range of 0 to 36 pg/microg of fSC of IgA and were higher in infants with severe pulmonary disorders compared with those in infants in the control group ($p < 0.02$). Urinary concentrations did not discriminate between sick infants and infants in the control group.

CT Check Tags: Human; Support, Non-U.S. Gov't
Biological Markers: AN, analysis
***Dinoprost: AA, analogs & derivatives**
Dinoprost: AN, analysis
Dinoprost: UR, urine
Exudates and Transudates: CH, chemistry
Immunoenzyme Techniques
Infant, Newborn
***Lipid Peroxidation**
*Lung Diseases: PP, physiopathology
*Respiratory Distress Syndrome: PP, physiopathology
Respiratory Distress Syndrome: UR, urine
Trachea

RN **155976-51-5 (8-isoprostane); 551-11-1 (Dinoprost)**
CN 0 (Biological Markers)

L161 ANSWER 4 OF 13 MEDLINE
AN 1998073662 MEDLINE
DN 98073662 PubMed ID: 9409197
TI **Isoprostanes**: potential markers of oxidant stress in atherothrombotic disease.
AU Patrono C; FitzGerald G A
CS Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia 19104-6100, USA.
NC 1P50HL54500 (NHLBI)
MO1 RR 00040 (NCRR)
SO ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, **(1997 Nov)** 17 (11) 2309-15. Ref: 65
Journal code: B89; 9505803. ISSN: 1079-5642.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980130
Last Updated on STN: 19980130
Entered Medline: 19980122
AB **Isoprostanes** are emerging as a new class of biologically active products of arachidonic acid metabolism of potential relevance to human vascular disease. Their formation in vivo seems to reflect primarily, if not exclusively, a nonenzymatic process of lipid peroxidation. Enhanced urinary excretion of 8-iso-PGF2 alpha has been described in association with cardiac reperfusion injury and with cardiovascular risk factors, including cigarette smoking, diabetes mellitus, and hypercholesterolemia. Besides providing a likely noninvasive index of lipid peroxidation in these settings, measurements of specific F2 **isoprostanes** in urine may provide a sensitive biochemical end point for dose-finding studies of natural and synthetic inhibitors of lipid peroxidation. Although the biological effects of 8-iso-PGF2 alpha in vitro suggest that it and other isoeicosanoids may modulate the functional consequences of lipid peroxidation, evidence that this is likely in vivo remains inadequate at this time.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antioxidants: PD, pharmacology
*Arteriosclerosis: ME, metabolism
Biological Markers
Cardiovascular Diseases: EP, epidemiology

Cardiovascular Diseases: ME, metabolism
Diabetes Mellitus: ME, metabolism
Dinoprost: AA, analogs & derivatives
Dinoprost: PD, pharmacology
Dinoprost: UR, urine
Free Radicals
Hyperlipidemia: ME, metabolism
Immunoassay
Indicator Dilution Techniques
***Lipid Peroxidation**
Mass Fragmentography
***Oxidative Stress**
Platelet Aggregation: DE, drug effects
***Prostaglandins F: AN, analysis**
Risk Factors
*Thrombosis: ME, metabolism
Vasoconstrictor Agents: PD, pharmacology
RN **551-11-1 (Dinoprost)**
CN 0 (8-**isoprostaglandin** F2alpha); 0 (Antioxidants); 0 (Biological Markers); 0 (Free Radicals); 0 (**Prostaglandins** F); 0 (Vasoconstrictor Agents)

L161 ANSWER 5 OF 13 MEDLINE
AN 1998040949 MEDLINE
DN 98040949 PubMed ID: 9373618
TI The **isoprostanes**: unique bioactive products of lipid peroxidation.
AU Morrow J D; Roberts L J
CS Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232-6602, USA.
NC DK48837 (NIDDK)
GM15431 (NIGMS)
GM42056 (NIGMS)
SO PROGRESS IN LIPID RESEARCH, **(1997 Mar)** 36 (1) 1-21. Ref: 94
Journal code: PZ7; 7900832. ISSN: 0163-7827.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971208
AB The discovery of IsoPs as products of non-enzymatic lipid peroxidation has opened up new areas of investigation regarding the role of free radicals in human physiology and pathophysiology. The quantification of IsoPs as markers of oxidative stress status appears to be an important advance in our ability to explore the role of free radicals in the pathogenesis of human disease. A drawback related to this, however, has been lack of more facile and less expensive methods than mass spectrometry for the measurement of IsoPs. On the other hand, the recent introduction of immunoassay methods for measurement of IsoPs may alleviate this problem, provided they are specific and reliable. If this is the case, immunoassay methodology will most likely lead to an expansion of the use of measurements of IsoPs to assess oxidative stress status in vivo. Another need in the field of free radical medicine is information regarding the clinical pharmacology of antioxidant agents. Because of the evidence implicating free radicals in the pathogenesis of a number of human diseases, large clinical trials are planned or underway to assess whether antioxidants can either prevent the development or ameliorate the pathology of certain human disorders. However, data regarding the most effective doses and combination of antioxidant agents to use in these clinical trials is lacking. As mentioned previously, administration of antioxidants suppresses the formation of IsoPs, even in normal

individuals. Thus, measurement of IsoPs may provide a valuable approach to defining the clinical pharmacology of antioxidants. In addition to being markers of oxidative stress, at least two IsoPs possess potent biological activity. The availability of additional IsoPs in synthetic form should broaden our knowledge concerning the role of these molecules as mediators of oxidant stress. Moreover, information regarding the nature of the receptor(s) that mediate the biological actions of IsoPs will be of considerable importance to the development of specific antagonists or agonists of the biological actions of IsoPs. Despite the fact that considerable information has been obtained since the initial report of the discovery of IsoPs, much remains to be understood about these molecules. With continued research in this area, we believe that much new information will emerge that will open up additional important new areas for future investigation.

CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Biological Markers
Dinoprost: AA, analogs & derivatives
Dinoprost: CH, chemistry
Dinoprost: ME, metabolism
Free Radicals
Isomerism
Leukotrienes: ME, metabolism
***Lipid Peroxidation**
***Oxidative Stress**
***Prostaglandins: ME, metabolism**
Receptors, Prostaglandin: ME, metabolism
Thromboxanes: ME, metabolism

RN **155976-51-5 (8-isoprostane); 551-11-1 (Dinoprost)**

CN 0 (Biological Markers); 0 (Free Radicals); 0 (Leukotrienes); 0 (**Prostaglandins**); 0 (Receptors, **Prostaglandin**); 0 (Thromboxanes); 0 (**prostaglandin** F2alpha receptor)

L161 ANSWER 6 OF 13 MEDLINE
AN 97474772 MEDLINE
DN 97474772 PubMed ID: 9329967
TI Localization of distinct F2-**isoprostanes** in human atherosclerotic lesions.
CM Erratum in: J Clin Invest 1997 Nov 15;100(10):2637
AU Pratico D; Iuliano L; Mauriello A; Spagnoli L; Lawson J A; Rokach J; Maclouf J; Violi F; FitzGerald G A
CS The Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA.
NC HL-54500 (NHLBI)
SO JOURNAL OF CLINICAL INVESTIGATION, **(1997 Oct 15)** 100 (8) 2028-34.
Journal code: HS7; 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 19990129
Entered Medline: 19971120
AB F2-**Isoprostanes** are **prostaglandin** (PG) isomers formed in situ in cell membranes by peroxidation of arachidonic acid. 8-epi PGF2alpha and IPF2alpha-I are F2-**isoprostanes** produced in humans which circulate in plasma and are excreted in urine. Measurement of F2-**isoprostanes** may offer a sensitive, specific, and noninvasive method for measuring oxidant stress in clinical settings where reactive **oxygen** species are putatively involved. We determined whether **isoprostanes** were present in human atherosclerotic lesions, where lipid peroxidation is thought to occur in vivo. 8-epi PGF2alpha ranged from 1.310-3.450 pmol/micromol phospholipid in atherectomy specimens compared with 0.045-0.115 pmol/micromol phospholipid ($P < 0.001$) in vascular tissue devoid of atherosclerosis. Corresponding values of

IPF2alpha-I were 5.6-13.8 vs. 0.16-0.44 pmol/micromol phospholipid (P < 0.001). Levels of the two **isoprostanes** in vascular tissue were highly correlated (r = 0.80, P < 0.0001). Immunohistochemical studies confirmed that foam cells adjacent to the lipid necrotic core of the plaque were markedly positive for 8-epi PGF2alpha. These cells were also reactive with anti-CD68, an epitope specific for human monocyte/macrophages. 8-epi PGF2alpha immunoreactivity was also detected in cells positive for anti-alpha-smooth muscle actin antibody, which specifically recognizes vascular smooth muscle cells. Our results indicate that 8-epi PGF2alpha and IPF2alpha-I, two distinct F2-**isoprostanes** and markers of oxidative stress in vivo, are present in human atherosclerotic plaque. Quantitation of these chemically stable products of lipid peroxidation in target tissues, as well as in biological fluids, may aid in the rational development of antioxidant drugs in humans.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
Aged
Antigens, CD: AN, analysis
Antigens, Differentiation, Myelomonocytic: AN, analysis
Aorta: CH, chemistry
Aorta: PA, pathology
*Arteries: CH, chemistry
Arteries: PA, pathology
*Arteriosclerosis
Carotid Arteries: CH, chemistry
Carotid Arteries: PA, pathology
***Dinoprost: AA, analogs & derivatives**
Dinoprost: AN, analysis
Foam Cells: CH, chemistry
Isomerism
Lipid Peroxidation
Middle Age
Oxidative Stress
Phospholipids: AN, analysis
Pulmonary Artery: CH, chemistry
Pulmonary Artery: PA, pathology

RN **27415-26-5 (8-epi-prostaglandin F2alpha); 551-11-1 (Dinoprost)**

CN 0 (Antigens, CD); 0 (Antigens, Differentiation, Myelomonocytic); 0 (CD68 antigen); 0 (Phospholipids)

L161 ANSWER 7 OF 13 MEDLINE
AN 97131154 MEDLINE
DN 97131154 PubMed ID: 8976806
TI Plasma and urinary 8-iso-**prostane** as an indicator of lipid peroxidation in pre-eclampsia and normal pregnancy.
AU Barden A; Beilin L J; Ritchie J; Croft K D; Walters B N; Michael C A
CS University Department of Medicine, Royal Perth Hospital, Australia.
SO CLINICAL SCIENCE, **(1996 Dec)** 91 (6) 711-8.
Journal code: DIZ; 7905731. ISSN: 0143-5221.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199701
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970114
AB 1. This study was designed to seek evidence for excessive lipid peroxidation in pre-eclamptic women using 8-iso-**prostane** as a novel bioactive marker of lipid peroxidation in vivo. Plasma free, total and urinary 8-iso-**prostane** were measured in 20 women with proteinuric pre-eclampsia, and compared with 18 age- and gestation-matched pregnant control subjects, before delivery and at 6 weeks post-partum. 2. Plasma free 8-iso-**prostane** was significantly elevated in the

pre-eclamptic women compared with control subjects before delivery, and fell to control levels post-partum. Conversely, levels in women with normal pregnancy rose post-partum. 3. Total plasma 8-iso-**prostane** levels were not significantly elevated in pre-eclamptic women compared with control subjects during pregnancy, but fell significantly in the pre-eclamptic women post-partum, suggesting that they had relatively higher levels compared with their non-pregnant state. 4. Urinary 8-iso-**prostane** excretion was significantly lower in the pre-eclamptic women compared with control subjects during pregnancy, suggesting that renal clearance of 8-iso-**prostane** is impaired in pre-eclampsia. 5. Increased levels of plasma free 8-iso-**prostane** in pre-eclampsia could be due to an increase in lipid peroxidation, an increase in phospholipase A2 activity or a reduction in renal clearance of 8-iso-**prostane**, or a combination of all three. The potent direct and indirect vasoconstrictor actions of 8-iso-**prostane** may contribute to the pathogenesis of pre-eclampsia.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't
Adult
Biological Markers: BL, blood
Biological Markers: UR, urine
***Dinoprost: AA, analogs & derivatives**
Dinoprost: BL, blood
Dinoprost: ME, metabolism
Dinoprost: UR, urine
***Lipid Peroxidation: PH, physiology**
Pre-Eclampsia: BL, blood
*Pre-Eclampsia: ME, metabolism
Pre-Eclampsia: UR, urine
Pregnancy: BL, blood
*Pregnancy: ME, metabolism
Pregnancy: UR, urine
Puerperium: BL, blood
Puerperium: UR, urine

RN **155976-51-5 (8-isoprostane); 551-11-1 (Dinoprost)**
CN 0 (Biological Markers)

L161 ANSWER 8 OF 13 MEDLINE
AN 97068997 MEDLINE
DN 97068997 PubMed ID: 8912185
TI A reliable and sensitive enzyme immunoassay method for measuring 8-**isoprostaglandin** F2 alpha: a marker for lipid peroxidation after experimental brain injury.
AU Hoffman S W; Roof R L; Stein D G
CS Brain Research Laboratory, Rutgers University, Newark, NJ 07102, USA.
SO JOURNAL OF NEUROSCIENCE METHODS, **(1996 Oct)** 68 (2) 133-6.
Journal code: K9V; 7905558. ISSN: 0165-0270.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
ED Entered STN: 19970313
Last Updated on STN: 19970313
Entered Medline: 19970228
AB The objectives of this study were to determine (1) if levels of 8-**isoprostaglandin** F2 alpha (8-isoPGF2 alpha), a non-enzymatically produced **prostaglandin**, were increased after cortical contusion and (2) if enzyme immunoassay (EIA) could be used to quantify 8-isoPGF2 alpha levels. 24 h after the contusion there was a significant rise in 8-isoPGF2 alpha compared to control levels. The levels returned to baseline by 72 h postinjury. The results show that this EIA method is a reliable and sensitive technique for measuring brain lipid peroxidation.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Biological Markers
*Brain Injuries: ME, metabolism
***Dinoprostone: ME, metabolism**

*Immunoassay: MT, methods
***Lipid Peroxidation: PH, physiology**
Rats
Rats, Sprague-Dawley
RN **363-24-6 (Dinoprostone)**
CN 0 (Biological Markers)

L161 ANSWER 9 OF 13 MEDLINE
AN 95250494 MEDLINE
DN 95250494 PubMed ID: 7732838
TI The **isoprostanes**: novel markers of lipid peroxidation and potential mediators of oxidant injury.
AU Roberts L J 2nd; Morrow J D
CS Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232, USA.
NC ES00267 (NIEHS)
GM42056 (NIGMS)
SO ADVANCES IN PROSTAGLANDIN, THROMBOXANE, AND LEUKOTRIENE RESEARCH, **(1995)** 23 219-24.
Journal code: 2PC; 8211444. ISSN: 0732-8141.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
ED Entered STN: 19950608
Last Updated on STN: 19950608
Entered Medline: 19950531
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Arachidonic Acids: AN, analysis
Biological Markers
***Lipid Peroxidation**
Molecular Structure
*Oxidants: TO, toxicity
Reference Values
Stereoisomerism
CN 0 (Arachidonic Acids); 0 (Biological Markers); 0 (Oxidants)

L161 ANSWER 10 OF 13 MEDLINE
AN 95126393 MEDLINE
DN 95126393 PubMed ID: 7825845
TI **Isoprostanes**. Novel markers of endogenous lipid peroxidation and potential mediators of oxidant injury.
AU Roberts L J 2nd; Morrow J D
CS Department of Pharmacology, Vanderbilt University, Nashville, Tennessee 37232.
NC GM42056 (NIGMS)
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, **(1994 Nov 15)** 744 237-42. Ref: 17
Journal code: 5NM; 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199502
ED Entered STN: 19950223
Last Updated on STN: 19950223
Entered Medline: 19950214
AB It was recently discovered that a series of structurally unique **prostaglandin** F2-like compounds (F2-**isoprostanes**) capable of exerting potent biological activity are produced in vivo in humans by a noncyclooxygenase mechanism involving free radical catalyzed peroxidation of arachidonic acid. Considerable evidence has been obtained

suggesting that quantification of F2-**isoprostanes** represents an important advance in our ability to assess oxidant status in vivo in humans. This has allowed us to implicate oxidant stress in the pathogenesis of human disease-for example, the hepatorenal syndrome. In addition to the F2-**isoprostanes**, we recently discovered that E-ring and D-ring **isoprostanes** are also produced in abundance in vivo by rearrangement of the **isoprostane** endoperoxide intermediates. We have also been able to demonstrate that one of the E2-**isoprostanes**, 8-epi-PGE2, is a potent renal vasoconstrictor in the rat. Insights into factors that may influence the formation of E2/D2-**isoprostanes** relative to F2-**isoprostanes** should be important in advancing our understanding of the biological consequences of the formation of **isoprostanes** in vivo.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Biological Markers
Dinoprost: AA, analogs & derivatives
***Dinoprost: ME, metabolism**
Lipid Peroxidation

RN **27415-26-5 (8-epi-prostaglandin F2alpha); 551-11-1 (Dinoprost)**

CN 0 (Biological Markers)

L161 ANSWER 11 OF 13 MEDLINE

AN 95045316 MEDLINE

DN 95045316 PubMed ID: 7957003

TI Diet and oxidative stress in breast, colon and **prostate** cancer patients: a case-control study.

AU Hietanen E; Bartsch H; Bereziat J C; Camus A M; McClinton S; Eremin O; Davidson L; Boyle P

CS Department of Clinical Physiology, Turku University Hospital, Finland.

SO EUROPEAN JOURNAL OF CLINICAL NUTRITION, **(1994 Aug)** 48 (8) 575-86.
Journal code: EJC; 8804070. ISSN: 0954-3007.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199412

ED Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941227

AB OBJECTIVE: To study the changes in pro-oxidant-antioxidant status in breast, colon and **prostate** cancer patients as compared to respective controls. DESIGN: Cross-sectional case-control study. The pro-oxidant status was measured by analysing alkanes (ethane and pentane) in exhaled air and lipid peroxidation (as malonaldehyde) in blood samples. The antioxidant capacity was measured by studying blood glutathione concentration, vitamin concentrations and serum antioxidant capacity in liposomes in vitro. SETTING: Aberdeen hospitals. SUBJECTS: Breast, **prostate** and colon cancer cases, and age- and sex-matched control patients (hospitalized for a benign disease). Breast cancer patients were females, **prostate** cancer patients were males and colon cancer patients were both males and females. Controls were age-matched to within 5 years, sex-matched and matched for smoking habits. RESULTS: The dietary study suggested a higher monoene and polyene fat intake in **prostate** cancer than in controls while in other cancer patients no significant differences were found. Breast and colon cancer patients tended to have lower vitamin intakes than controls. Pentane concentration in exhaled air increased in breast cancer patients as compared to respective controls. In serum total antioxidant capacity no significant differences were found. Both breast and colon cancer patients showed decreased C18:2 and C20:4 fatty acid concentrations in red blood cells while C22:6 concentration was elevated in breast cancer patients. CONCLUSIONS: Oxidative stress may be associated with malignant diseases, suggesting the importance of simultaneous analysis of pro- and antioxidation in the search of mechanistic parameters leading to the

tumour formation.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Aged, 80 and over
Biological Markers
Breast Neoplasms: EP, epidemiology
*Breast Neoplasms: ET, etiology
Breast Neoplasms: ME, metabolism
Breast Neoplasms: PA, pathology
Breath Tests
Case-Control Studies
Colonic Neoplasms: EP, epidemiology
*Colonic Neoplasms: ET, etiology
Colonic Neoplasms: ME, metabolism
Colonic Neoplasms: PA, pathology
Cross-Sectional Studies
*Diet: AE, adverse effects
Ethane: AN, analysis
Glutathione: BL, blood
Lipid Peroxidation
Malondialdehyde: BL, blood
Matched-Pair Analysis
Middle Age
Neoplasm Staging
***Oxidative Stress: PH, physiology**
Pentanes: AN, analysis
Pilot Projects
Prostatic Neoplasms: EP, epidemiology
***Prostatic Neoplasms: ET, etiology**
Prostatic Neoplasms: ME, metabolism
Prostatic Neoplasms: PA, pathology
Risk Factors
Vitamins: BL, blood
RN 109-66-0 (pentane); 542-78-9 (Malondialdehyde); 70-18-8 (Glutathione); 74-84-0 (Ethane)
CN 0 (Biological Markers); 0 (Pentanes); 0 (Vitamins)

L161 ANSWER 12 OF 13 MEDLINE
AN 93121868 MEDLINE
DN 93121868 PubMed ID: 1478157
TI Possible relevance of lipid peroxidation and thromboxane production to the initiation and/or evolution of microangiopathy in non-hyperlipidemic type 2 diabetes mellitus.
AU Katoh K
CS Third Department of Internal Medicine, Fukushima Medical College, Japan.
SO DIABETES RESEARCH AND CLINICAL PRACTICE, **(1992 Nov)** 18 (2) 89-98.
Journal code: EBI; 8508335. ISSN: 0168-8227.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
ED Entered STN: 19930226
Last Updated on STN: 19930226
Entered Medline: 19930209
AB To investigate the possible relevance of free radicals and **prostanoids** to the mode of initiation and/or evolution of microangiopathy in diabetes mellitus, we measured serum lipid peroxides (LPO), an accepted index of intravascular free radicals, and plasma 11-dehydrothromboxane B2 (11-dehydro-TXB2), a stable metabolite of vasoactive thromboxane A2 released from platelets, in 95 patients with normolipidemic type 2 (non-insulin-dependent) diabetes mellitus at different stages of the disease. In general, either LPO or 11-dehydro-TXB2 was significantly greater in the patients, as a group, than in the matched

controls (3.82 vs. 2.65 nmol/ml, P < 0.01 for LPO; and 17.3 vs. 5.8 pg/ml, P < 0.01 for 11-dehydro-TXB2). In patients, both LPO and 11-dehydro-TXB2 increased according to the severity of their diabetic retinopathy. A highly significant positive correlation existed between the LPO values and 11-dehydro-TXB2 in the patients (r = 0.64, P < 0.0001), while there was no such relationship in the controls (r = 0.18, P = NS). No difference in serum levels of apolipoproteins A-I, A-II, B, C-II, C-III, or E was observed between the patients and controls. Short-term glycemic control (25 cal/kg of standardized body weight/day, for 8 weeks) resulted in a small but significant reduction in LPO (4.2 vs. 4.6 nmol/ml, control; P < 0.05) without alteration in 11-dehydro-TXB2. There was a tendency towards deterioration in LPO according to the improvement in glycemic control. These results appear consistent with the view that, in addition to LPO, the release of TXA2 from activated platelet in the human circulation could be an important factor for the initiation and/or evolution of microangiopathy in diabetic patients even when they are not apparently hyperlipidemic. Further, the results of the present study emphasize the notion that more tight control of serum lipids is worthy of serious consideration in preventing the advance of diabetic microangiopathy.

CT Check Tags: Female; Human; Male
Aged
*Apolipoproteins: BL, blood
Biological Markers: BL, blood
Blood Glucose: AN, analysis
Cholesterol: BL, blood
Diabetes Mellitus, Non-Insulin-Dependent: BL, blood
*Diabetes Mellitus, Non-Insulin-Dependent: PP, physiopathology
*Diabetic Angiopathies: BL, blood
*Diabetic Angiopathies: DI, diagnosis
Diabetic Nephropathies: BL, blood
Diabetic Retinopathy: BL, blood
Free Radicals
Hemoglobin A, Glycosylated: AN, analysis
***Lipid Peroxidation**
*Lipid Peroxides: BL, blood
Lipoproteins, HDL Cholesterol: BL, blood
Middle Age
Reference Values
*Thromboxane B2: AA, analogs & derivatives
Thromboxane B2: BL, blood
Triglycerides: BL, blood

RN 54397-85-2 (Thromboxane B2); 57-88-5 (Cholesterol); 67910-12-7 (11-dehydro-thromboxane B2)

CN 0 (Apolipoproteins); 0 (Biological Markers); 0 (Blood Glucose); 0 (Free Radicals); 0 (Hemoglobin A, Glycosylated); 0 (Lipid Peroxides); 0 (Lipoproteins, HDL Cholesterol); 0 (Triglycerides)

L161 ANSWER 13 OF 13 MEDLINE
AN 91323757 MEDLINE
DN 91323757 PubMed ID: 1907587
TI Quantification of noncyclooxygenase derived **prostanoids** as a marker of oxidative stress.
AU Morrow J D; Roberts L J 2nd
CS Department of Pharmacology, Vanderbilt University, Nashville, TN 37232-6602.
NC GM 07569 (NIGMS)
GM 42056 (NIGMS)
SO FREE RADICAL BIOLOGY AND MEDICINE, **(1991)** 10 (3-4) 195-200.
Journal code: FRE; 8709159. ISSN: 0891-5849.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199109
ED Entered STN: 19910929
Last Updated on STN: 19910929

Entered Medline: 19910912

AB Recently, we discovered there is a unique class of **prostaglandin** F2-like compounds that are formed in vitro from arachidonoyl-containing lipids in plasma by a free radical-catalyzed mechanism. More recent studies have elucidated that these **prostanoids** are also produced in vivo in humans by a similar noncyclooxygenase mechanism. Levels of these PGF2 compounds detected by a mass spectrometric assay in normal human plasma and urine range from approximately 5-50 pg/mL and 500-3000 pg/mg creatinine, respectively. Circulating levels of the compounds were shown to increase by as much as 200-fold in animal models of free radical-induced lipid peroxidation. These results suggest that quantification of these **prostanoids** may provide a new approach to assess oxidative stress in vivo in humans. Potential advantages of this approach are that the mass spectrometric assay has a high degree of sensitivity, accuracy, and specificity and the assay can be used to quantitate these compounds in a variety of biological fluids. In addition, quantification of these compounds is of interest because these compounds possess biological activity. Disadvantages of the assay are the potential of ex vivo formation of these compounds in biological fluids containing lipids and, further, these compounds must be differentiated from PGF2 compounds that are formed via the **cyclooxygenase** enzyme. In addition, because the levels of these compounds in normal human plasma and urine are relatively high, assaying these compounds in circulating plasma and urine may be somewhat insensitive for the detection of increased production at isolated sites of oxidant injury within the body, in which case sampling near localized sites of their formation may be required.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Biological Markers
Dinoprost: BL, blood
Dinoprost: UR, urine
Free Radicals
Lipid Peroxidation
***Oxygen: ME, metabolism**
Prostaglandin-Endoperoxide Synthase: BL, blood
Prostaglandin-Endoperoxide Synthase: UR, urine
***Prostaglandins: AN, analysis**
Prostaglandins: BL, blood
Prostaglandins: UR, urine
Stress

RN **551-11-1 (Dinoprost); 7782-44-7 (Oxygen)**

CN 0 (Biological Markers); 0 (Free Radicals); 0 (**Prostaglandins**); EC 1.14.99.1 (**Prostaglandin**-Endoperoxide Synthase)

=> d his

(FILE 'HOME' ENTERED AT 07:14:09 ON 29 JAN 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 07:14:19 ON 29 JAN 2002
E ISOPROSTANE

```
L1          558 S E1-E9
L2            3 S ISO PROSTAN?
L3          559 S L1,L2
L4            0 S (IPF2ALPHA OR IPF2ALFA)()III
L5            0 S IPF()(2ALPHA OR 2ALFA)()III
L6            0 S IPF()2()(ALPHA OR ALFA)()III
L7            0 S L3 (L) (2ALPHA OR 2ALFA OR 2()(ALPHA OR ALFA))(L)III
L8            0 S L3 (L) (2ALPHA OR 2ALFA OR 2()(ALPHA OR ALFA))(L)VI
L9            0 S L3 (L) (2ALPHA OR 2ALFA OR 2()(ALPHA OR ALFA))(L)VI
L10           0 S IPF()2()(ALPHA OR ALFA)()VI
L11           0 S IPF()(2ALPHA OR 2ALFA)()VI
L12           2 S (IPF2ALPHA OR IPF2ALFA)()VI
L13          30 S IPF2(L)(ALPHA OR ALFA)(L)III
L14          18 S IPF2(L)(ALPHA OR ALFA)(L)VI
```

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L15          39 S L13,L14
L16          12 S L15 (L) 8 12 ISO

     FILE 'REGISTRY' ENTERED AT 07:24:25 ON 29 JAN 2002
L17           3 S 190664-75-6 OR 180469-63-0 OR 214894-56-1
                E IPF2.ALPHA.-III/CN
L18           1 S E3
L19           2 S E2,E4
L20           1 S L17 NOT L18,L19
L21           1 S L18,L19 NOT L17
                E ISOPROSTANE/CN
L22           3 S E4-E6
L23           1 S E2 NOT L22
                E 8,12-ISO/CN
L24           5 S L17-L23
L25           1 S 7782-44-7
                E CYCLOOXYGNASE/CN
                E CYCLOOXYGENASE/CN
L26           1 S E3
L27           2 S E6,E7
L28           3 S L26,L27

     FILE 'HCAPLUS' ENTERED AT 07:28:57 ON 29 JAN 2002
L29         321 S L24
L30          23 S L17
L31          44 S L15,L16,L30
L32         665 S L3,L29
L33          40 S L32 AND L31
L34          44 S L31,L33
L35         625 S L32 NOT L34
                E FFITZGERALD G/AU
                E FITZGERALD G/AU
L36         274 S E3,E4,E15-E19
                E ROKACH J/AU
L37         251 S E3,E4,E6-E8
                E PRATICO D/AU
L38          69 S E3,E4
                E TROJANOWSKI J/AU
L39         251 S E3-E5,E9-E12
L40         766 S L36-L39
L41          32 S L40 AND L34
L42          41 S L40 AND L35
L43          73 S L41,L42
L44          25 S L43 AND (QUANTITATIVE OR QUANTIFICATION OR EVIDENCE OR ASSESS
L45          14 S L43 AND REVIEW/ST
L46         115 S (L17 OR L24)(L)(OCCU/RL OR ANST/RL OR ANT/RL)
L47          16 S L43 AND L46
L48          35 S L44,L45,L47
L49          21 S L48 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L50          20 S L49 NOT 128:58619/DN
L51          66 S L40 AND P/DT
L52           1 S L51 AND L34,L35
L53          10 S L25 AND L40
L54          39 S L28 AND L40
L55           3 S L53,L54 AND L50
L56          21 S L49,L52,L55

     FILE 'REGISTRY' ENTERED AT 08:56:13 ON 29 JAN 2002
L57           1 S 78-44-4

     FILE 'REGISTRY' ENTERED AT 08:56:35 ON 29 JAN 2002

     FILE 'HCAPLUS' ENTERED AT 08:57:33 ON 29 JAN 2002
L58         165 S L57
L59           6 S ISOPROTAN# OR ISOPROTHAN# OR ISO()(PROTAN# OR PROTHAN#)
L60         168 S CARISOPRODOL#
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L61         231 S L58-L60
L62           1 S L40 AND L61
L63          21 S L56,L62
L64          21 S L63 AND L1-L16,L29-L56,L58-L63
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 09:03:45 ON 29 JAN 2002
L65           7 S E1-E7
L66          10 S L24,L28,L57,L65

     FILE 'REGISTRY' ENTERED AT 09:04:35 ON 29 JAN 2002

     FILE 'HCAPLUS' ENTERED AT 09:04:46 ON 29 JAN 2002

     FILE 'BIOSIS' ENTERED AT 09:06:23 ON 29 JAN 2002
                E FITZGERALD G/AU
L67         537 S E3,E4,E21-E23
                E ROKACH J/AU
L68         185 S E3,E4,E6-E8
                E PRATICO D/AU
L69          92 S E3-E5
                E TROJANOWSKI J/AU
L70         579 S E3-E6,E9-E13
L71        1288 S L67-L70
L72          84 S L57
L73          90 S L59 OR L60
L74           6 S L24
L75         749 S L3
L76          44 S L4-L16
L77          89 S L71 AND L72-L76
L78          31 S L77 AND 00520/CC
L79          31 S L77 AND (CONFERENCE OR CONGRESS OR POSTER OR SYMPOS? OR MEETI
L80          31 S L78,L79
L81          15 S L80 AND PY<=1998
                SEL DN AN 1 3 4 6 14 15
L82           9 S L81 NOT E1-E12

     FILE 'BIOSIS' ENTERED AT 09:13:24 ON 29 JAN 2002

     FILE 'WPIX' ENTERED AT 09:13:34 ON 29 JAN 2002
                E FITZGERALD G/AU
L83           8 S E3,E4
                E ROKACH J/AU
L84          74 S E3,E4
                E PRATICO D/AU
L85           1 S E3
                E TROJANOWSKI J/AU
L86          16 S E3,E4
                E ISOPROSTANE
L87           3 S E3,E4
L88           8 S L59 OR L60
                E CARISOPRODOL/DCN
                E E3+ALL
L89           5 S E2
L90           1 S L83-L86 AND L87-L89

     FILE 'WPIX' ENTERED AT 09:15:27 ON 29 JAN 2002
L91          14 S L87,L88,L89
L92          13 S L91 NOT L90
L93           2 S L92 AND (G01N OR C12Q)/IC,ICM,ICS

     FILE 'HCAPLUS' ENTERED AT 09:21:07 ON 29 JAN 2002
L94         230 S L61 NOT L64
L95         218 S L94 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L96           0 S L95 AND L34
L97           0 S L95 AND L35
```

L154	3	S	L151 AND (L28 OR COX# OR CYCLOOXYGENASE)
L155	45	S	L151 AND (L25 OR O2 OR OXYGEN)
L156	5	S	L153 AND L154,L155
L157	13	S	L153,L156
L158	9800	S	OXIDATIVE STRESS+NT/CT
L159	30	S	L158 AND L151
L160	6	S	L159 AND L157
L161	13	S	L157,L160
L162	0	S	L140 AND L158
L163	0	S	L140 AND STRESS?
L164	0	S	L140 AND L148
L165	0	S	L140 AND BIOLOGICAL MARKERS+NT/CT

US 0987076208P1

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Legal Date: 02-15-2002

No.	Doccode	Number of pages
1	SRNT	11

Total number of pages: 11

Remarks:

Order of re-scan issued on .....